```
Set     Items   Description
S1        192   (DENDRITIC)(20N)(THERAP? OR TREAT?)(30N)(CORRELAT? OR PRED-
            ICT?)
S2         96   RD S1 (unique items)
S3          0   S2 AND ATP
S4        459   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
S5         81   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)(10N)(A-
            DD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
S6         44   RD S5 (unique items)
S7         54   S2 AND (DISEASE? OR IMMUNITY OR VIRAL OR BACTERIAL OR CANC-
            ER?)
S8          3   S2 AND REVIEW?
S9       4023   (DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE OR
            ADMINIST?)
S10       302   S9 AND REVIEW?
S11       269   RD S10 (unique items)
S12        48   S11 AND PY=2002
S13        48   RD S12 (unique items)
S14        29   S11 AND PY=2003
S15        29   RD S14 (unique items)
S16        60   (DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE OR
            ADMINIST?)(20N)(CORRELAT? OR PREDICT?)
S17        33   RD S16 (unique items)
?
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        11jun03 11:00:32 User208760 Session D2316.1
             $0.32    0.090 DialUnits File1
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      $0.32  Estimated cost this search
      $0.32  Estimated total session cost   0.090 DialUnits

File 410:Chronolog(R)  1981-2003/Mar
       (c) 2003 The Dialog Corporation

       Set  Items  Description
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HILIGHT set on as ''
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       11jun03 11:00:37 User208760 Session D2316.2
            $0.00    0.071 DialUnits File410
     $0.00  Estimated cost File410
     $0.01  TELNET
     $0.01  Estimated cost this search
     $0.33  Estimated total session cost   0.161 DialUnits

SYSTEM:OS  - DIALOG OneSearch
  File   5:Biosis Previews(R)  1969-2003/Jun W2
         (c) 2003 BIOSIS
*File   5: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File  73:EMBASE  1974-2003/Jun W1
         (c) 2003 Elsevier Science B.V.
*File  73: Alert feature enhanced for multiple files, duplicates
removal, customized scheduling. See HELP ALERT.
  File 155:MEDLINE(R)  1966-2003/Jun W1
         (c) format only 2003 The Dialog Corp.
*File 155: Medline has been reloaded and accession numbers have
changed.  Please see HELP NEWS 155.
  File 399:CA SEARCH(R)  1967-2003/UD=13824
         (c) 2003 American Chemical Society
*File 399: Use is subject to the terms of your user/customer agreement.
Alert feature enhanced for multiple files, etc. See HELP ALERT.

      Set  Items  Description
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? s (dendritic)(20n)(therap? or treat?)(30n)(correlat? or predict?)
Processing
Processing
Processing
          98249  DENDRITIC
        5601623  THERAP?
        6042984  TREAT?
        1918476  CORRELAT?
        1055145  PREDICT?
     S1     192  (DENDRITIC)(20N)(THERAP? OR TREAT?)(30N)(CORRELAT? OR
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...examined 50 records  (100)
...examined 50 records  (150)
...completed examining records
     S2      96  RD S1 (unique items)
? s s2 and atp
             96  S2
         326980  ATP
     S3       0  S2 AND ATP
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          326980  ATP
           98249  DENDRITIC
         1129519  ANTIGEN
         3815635  PRESENT?
           65658  ANTIGEN(W)PRESENT?
           31425  APC?
      S4     459  (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
? s (atp)(20n)(dendritic or antigen(w)present? or apc?)(10n)(add? or stimulat? or
incubat? or cultur?)
Processing
Processing
          326980  ATP
           98249  DENDRITIC
         1129519  ANTIGEN
         3815635  PRESENT?
           65658  ANTIGEN(W)PRESENT?
           31425  APC?
         3346652  ADD?
         2099295  STIMULAT?
          558358  INCUBAT?
         2119842  CULTUR?
      S5      81  (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR
                  APC?)(10N)(ADD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
? rd s5
...examined 50 records  (50)
...completed examining records
      S6      44  RD S5 (unique items)
? t s6/7/all

 6/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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14115211   BIOSIS NO.: 200300109240
Sensitization of the Cardiac KATP Channel by Isoflurane: A Possible Role in
  Anesthetic-Induced Preconditioning.
AUTHOR: Gassmayr Susanne(a); Suzuki Akihiro(a); Stadnicka Anna(a); Kwok
  Wai-Meng(a); Bosnjak Zeljko(a)
AUTHOR ADDRESS: (a)Anesthesiology, Medical College of Wisconsin, Milwaukee,
  WI, USA**USA
JOURNAL: Anesthesiology Abstracts of Scientific Papers Annual Meeting (2001
):pAbstract No A-596 2002
MEDIUM: cd-rom
CONFERENCE/MEETING: 2001 Annual Meeting of the American Society of
Anesthesiologists  New Orleans, LA, USA  October 13-17, 2001
SPONSOR: American Society of Anesthesiologists Inc.
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Introduction: Volatile anesthetics have been shown to exert
  cardioprotective effects by mimicking ischemic preconditioning. However,
  the underlying cellular and molecular mechanisms may not be identical. In
  contrast to the mechanism involved in ischemic preconditioning, there is
  strong evidence that the sarcolemmal ATP sensitive potassium (KATP)
  channel plays an important role in anesthetic induced preconditioning (
  APC) of the heart (1). In addition, though protein kinase C
  (PKC) pathways have been shown to play pivotal roles in ischemic
  preconditioning, this involvement in APC has not been unequivocally
  defined. In the present study, we tested the hypotheses that isoflurane
  sensitizes the sarcolemmal KATP channel to pinacidil, a potassium channel
  opener, and that this mechanism involves a PKC pathway. Methods: Upon
  approval by the Institutional Animal Use and Care Committee, ventricular
  myocytes were isolated enzymatically from guinea pig hearts. Currents
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were recorded in the whole-cell configuration of the patch clamp technique under conditions designed to measure the KATP channel current. The external solution contained 5 mM K+, and 0.2 mM nisoldipine to block the L-type calcium channels. The pipette solution contained either 0.5 mM or 5 mM ATP. Membrane current was measured every 15 sec by applying a 100 ms voltage step to 0 mV from a holding potential of -40 mV. After 20 minutes of baseline control recordings to allow for cell dialysis with the pipette solution, isoflurane (0.55 mM) was added to the bath solution. After the steady state effects were recorded, the KATP channel opener, pinacidil (10 muM), was added in the presence of isoflurane. The same protocol was repeated in the presence of bisindolylmaleimide I (BIM, 200 nM), a selective inhibitor of PKC. In control experiments, the effects of pinacidil alone were also examined. Currents were normalized to cell capacitance to allow comparison among cells. Statistical analysis was performed using the Student's t-test. $P<0.05$ was considered significant and data are presented as mean+-SEM. Results: Under control conditions, KATP current density induced by pinacidil was 11.2+-1.7 pA/pF and 11.0+-4.0 pA/pF with 0.5 mM ATP and 5 mM ATP in the pipette, respectively (n=6). Pretreatment with isoflurane significantly ($p < 0.05$) increased the pinacidil induced KATP current density to 35.2+-5.2 pA/pF with 0.5 mM ATP. However, with an intracellular ATP of 5 mM, pretreatment with isoflurane did not significantly increase the pinacidil induced KATP current (19.6+-12.1 versus 11.0+-4.0 pA/pF). The PKC inhibitor BIM did not affect the sensitization by isoflurane observed with the lower intracellular ATP. Conclusion: The results from this study show that isoflurane sensitizes the cardiac sarcolemmal KATP channel to a potassium channel opener, pinacidil. This effect is ATP dependent, suggesting that under conditions of low intracellular ATP levels, isoflurane may be cardioprotective, whereas at physiologic ATP levels the sensitizing effect is suppressed. Our results also suggest that isoflurane sensitization of the KATP channel to pinacidil may not involve a PKC dependent pathway.

6/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

14114293 BIOSIS NO.: 200300108322
Anesthetic Preconditioning Triggered by Reactive Oxygen Species Improves Mitochondrial Function after Ischemia.
AUTHOR: Novalija Enis(a); Kevin Leo G(a); Henry Michele M(a); Eells Janis T (a); Stowe David F(a)
AUTHOR ADDRESS: (a)Anesthesiology, Physiology, Pharmacology and Toxicology, Medical College of Wisconsin, Milwaukee, WI, USA**USA
JOURNAL: Anesthesiology Abstracts of Scientific Papers Annual Meeting (2002):pAbstract No A-100 2002
MEDIUM: cd-rom
CONFERENCE/MEETING: 2002 Annual Meeting of the American Society of Anesthesiologists Orlando, FL, USA October 12-16, 2002
SPONSOR: American Society of Anesthesiologists Inc.
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Introduction: Anesthetic exposure before ischemia (anesthetic preconditioning, APC) reduces infarct size and reactive oxygen species (ROS) formation on reperfusion. We hypothesized that anesthetics cause formation of ROS to trigger APC. Indeed, we have shown that scavengers of ROS given only during APC pulses blocked protection and returned formation of ROS to control levels on reperfusion in isolated guinea pig hearts. The present study explored the role of APC in triggering protective mechanisms against ischemia-reperfusion injury via preservation of mitochondrial function. The impact of brief anesthetic exposure before ischemia and reperfusion on subsequent mitochondrial

bioenergetics may be an important event that initiates cardioprotection by APC. Methods: Guinea pig hearts (n=50) were isolated and perfused with crystalloid buffer at 55 mmHg and developed LVP was measured. Thirty hearts were subject to 30 min global ischemia and infarct size was measured at 120 min reperfusion. These hearts were untreated (CON), or treated with two 2-min sevoflurane (2.6 vol%, 0.36 mM) with/without 100 muM Tiron (APC, APC+TIR), a ROS scavenger, or TIR alone. TIR was infused 5 min before, during and 5 min after APC. All drugs were washed out for 15 min before ischemia. In a parallel study, twenty hearts underwent the same protocols, but hearts were removed at the first minute of reperfusion to determine ATP synthesis and ROS formation (fluorescence of carboxy-dichloro-dihydro-fluorescein, DCHF) in mitochondria isolated by differential centrifugation. Another group (SHAM) was not subject to ischemia and reperfusion. Data are means +- SEM (P< 0.05; * vs. CON). Results: At 120 min, LVP (mmHg) was improved and infarct size (% of total heart weight) was reduced after APC (55+-2*mmHg, 22+-2*%) vs. CON (22+-2 mmHg, 51+-3 %), **APC**+TIR (23+-3 mmHg, 48+-3 %), TIR (25+-3 mmHg, 52+-4 %), respectively. Mitochondrial ROS formation (a.u., 120 min **incubation**) and **ATP** synthesis rate (100 % SHAM), respectively, were SHAM (405+-22*a.u., 100*%) vs. **APC** (387+-59*a.u., 92+-2.6*%), CON (601+-92 a.u., 29+-2.5 %), **APC**+TIR (582+-43 a.u., 31+-2.4 %), TIR (585+-70 a.u., 31+-3.2 %). Conclusions: These results indicate that cardioprotection elicited by APC is likely due, at least in part, to ROS formation during exposure to sevoflurane because bracketing APC with a ROS scavenger blocked APC. Moreover, this study first shows that mitochondrial bioenergetics is better preserved (increased mitochondrial ATP synthesis) after APC. This may be due to less damage to the electron transport chain (reduced mitochondrial ROS formation) during ischemia and initial reperfusion.

6/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13570807 BIOSIS NO.: 200200199628
Dendritic cells exposed to extracellular adenosine triphosphate acquire the migratory properties of mature cells and show a reduced capacity to attract type 1 T lymphocytes.
AUTHOR: La Sala Andrea; Sebastiani Silvia; Ferrari Davide; Di Virgilio Francesco; Idzko Marco; Norgauer Johannes; Girolomoni Giampiero(a)
AUTHOR ADDRESS: (a)Instituto Dermopatico dell'Immacolata, IRCCS, Via Monti di Creta 104, 00167, Rome**Italy E-Mail: giro@idi.it
JOURNAL: Blood 99 (5):p1715-1722 March 1, 2002
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We previously reported that chronic **stimulation** with low, noncytotoxic doses of extracellular adenosine triphosphate (**ATP**) induced a distorted maturation of **dendritic** cells (DCs) and impaired their capacity to initiate T-helper (Th) 1 responses in vitro. Here, we examined the effects of **ATP** on chemokine-receptor expression and chemokine production by DCs. **ATP** strongly induced expression of CXC chemokine receptor 4 on both immature and lipopolysaccharide (LPS)-**stimulated** DCs and slightly up-regulated CC chemokine receptor (CCR) 7 on both DC types. In contrast, ATP reduced CCR5 expression on immature DCs. These effects were confirmed at both the messenger RNA and protein levels and were not produced by uridine triphosphate (UTP). Consistent with the changed receptor expression, ATP increased migration and intracellular calcium of immature and mature DCs to stromal-derived factor 1 (CXC ligand (CXCL) 12) and macrophage

inflammatory protein (MIP) 3beta (CC ligand (CCL) 19), whereas responses to MIP-1beta (CCL4) were reduced. DCs are an important source of chemokines influencing recruitment of distinct T-lymphocyte subsets. ATP, but not UTP, significantly reduced LPS-induced production of interferon-inducible protein 10 (CXCL10) and regulated upon activation, normal T-cell expressed and secreted chemokine (CCL5); increased secretion of macrophage-derived chemokine (CCL22); and did not change production of thymus and activation-regulated chemokine (CCL17). Consistent with these findings, supernatants from ATP-treated mature DCs attracted Th1 and T-cytotoxic 1 cells less efficiently, whereas migration of Th2 and T cytotoxic 2 cells was not affected. Our data suggest that ATP provides a signal for enhanced lymph node localization of DCs but that it may, at the same time, diminish the capacity of DCs to amplify type 1 immune responses.

6/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13293371 BIOSIS NO.: 200100500520
Purinoreceptors are involved in the control of acute morphine withdrawal.
AUTHOR: Capasso Anna(a); Loizzo Alberto
AUTHOR ADDRESS: (a)Department of Pharmaceutical Sciences, University of Salerno, Via Ponte Don Melillo, 84084, Fisciano, Salerno: annacap@unisa.it**Italy
JOURNAL: Life Sciences 69 (18):p2179-2188 September 21, 2001
MEDIUM: print
ISSN: 0024-3205
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The effects exerted by P1 and P2 purinoceptor agonists and antagonists on the acute opiate withdrawal induced by morphine were investigated in vitro. Following a 4 min in vitro exposure to morphine, the guinea-pig isolated ileum exhibited a strong contracture after the **addition** of naloxone. The P1 purinoceptor agonist, adenosine, was able dose-dependently to reduce morphine withdrawal whereas alpha,beta-methylene **ATP** (**APCPP**), a P2 purinoceptor agonist, increased morphine withdrawal. Caffeine, a P1 purinoceptor antagonist, was able significantly and in a concentration dependent manner to increase morphine withdrawal whereas quinidine, a P2 receptor antagonist, reduced it. The results of our experiments indicate that both P1 and P2 purinoceptor agonists and antagonists are able to influence opiate withdrawal in vitro, suggesting an important functional interaction between the purinergic system and opioid withdrawal.

6/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12927554 BIOSIS NO.: 200100134703
Molecular evolution of calcium-stimulated inositol trisphosphate 3-kinases.
AUTHOR: Schell M J; Letcher A J; Irvine R F
JOURNAL: Society for Neuroscience Abstracts 26 (1-2):pAbstract No-8205 2000
MEDIUM: print
CONFERENCE/MEETING: 30th Annual Meeting of the Society of Neuroscience New Orleans, LA, USA November 04-09, 2000
SPONSOR: Society for Neuroscience
ISSN: 0190-5295

RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The capacity of neocortex to produce the higher inositol polyphosphates (InsP4-InsP8) exceeds other tissues, but the functional and signalling roles of these molecules remain incompletely defined. Neuronal Ins(1,4,5)P3 calcium signalling is shaped partially via Ins(1,4,5)P3 3-kinases, which are highly **stimulated** by calcium, enriched in **dendritic** spines, and produce the putative second messenger Ins(1,3,4,5)P4. We have investigated a cDNA called phosphate uptake **stimulator**, or PiUS, which contains inositol polyphosphate- and **ATP**-binding motifs in its primary structure that resemble analogous ones in Ins(1,4,5)P3 3-kinases. However, when PiUS protein was expressed, it did not exhibit Ins(1,4,5)P3 3-kinase activity but rather a robust and selective InsP6-kinase activity, which was insensitive to calcium. Phylogenetic analyses define a conserved inositol-binding motif that recapitulates a single exon in both plant and animal evolution. Different combinations of modules around this exon appear to create inositide kinases having different substrate specificities. Whereas yeasts and plants phosphorylate Ins(1,4,5)P3 chiefly through a calcium-insensitive 6-kinase pathway found in the nucleus, vertebrates use a cytosolic calcium-stimulatable Ins(1,4,5)P3 3-kinase activity. The rapidly-evolving calmodulin binding motif and CAM kinase II phosporlation site, which confer a robust calcium sensitivity, are a recent innovation in higher animals. Genomic analyses support the idea that the capacity to produce Ins(1,3,4,5)P4 has evolved in concert with IP3-mediated calcium signalling.

6/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12795388 BIOSIS NO.: 200100002537
Chronic **stimulation** of **dendritic** cells with **ATP** results in impaired production of IL-12 and reduced ability to initiate Th1 responses.
AUTHOR: la Sala A(a); Ferrari D; Corinti S(a); Cavani A(a); Di Virgilio F; Girolomoni G(a)
AUTHOR ADDRESS: (a)Laboratory of Immunology, Istituto Dermopatico dell'Immacolata, IRCCS, Rome**Italy
JOURNAL: Journal of Investigative Dermatology 115 (3):p569 September, 2000
MEDIUM: print
CONFERENCE/MEETING: Abstracts for the 30th European Society for Dermatological Research Annual Meeting Berlin, Germany September 21-23, 2000
ISSN: 0022-202X
RECORD TYPE: Citation
LANGUAGE: English
SUMMARY LANGUAGE: English

6/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12793667 BIOSIS NO.: 200100000816
The transport mechanism of metallothionein is different from that of classical NLS-bearing protein.
AUTHOR: Nagano Takayuki; Itoh Norio(a); Ebisutani Chikara; Takatani Tomoka; Miyoshi Tomoya; Nakanishi Tsuyoshi; Tanaka Keiichi
AUTHOR ADDRESS: (a)Department of Toxicology, Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamada-oka, Suita, Osaka,

565-0871: n-itoh@phs.osaka-u.ac.jp**Japan
JOURNAL: Journal of Cellular Physiology 185 (3):p440-446 December, 2000
MEDIUM: print
ISSN: 0021-9541
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: A nuclear localization signal (NLS) has been detected in several nuclear proteins. Classical NLS-mediated nuclear pore targeting is performed by using the cytosolic factors, importin alpha and importin beta, whereas nuclear translocation requires the small GTPase, Ran. In the present study, we demonstrated that nuclear localization of metallothionein (MT) differs from that of classical NLS-mediated substrates. In digitonin-permeabilized BALB/c3T3 cells, biotinylated MT was localized in the nucleus in the presence of **ATP** and erythrocyte cytosol in the same manner as for SV40 large T NLS-conjugated allophycocyanin (**APC**-NLS). Under **ATP**-free conditions, nuclear rim-binding was observed in both transport substrates. Rim-binding of labeled MT was competitively inhibited by the **addition** of an excess amount of unlabeled MT. Different elution profiles were observed for the localization-promoting activities of MT in the cytosol compared to those of APC-NLS. Furthermore, nuclear localization of MT was determined to be a wheat germ agglutinin-insensitive, GTPgammaS-sensitive, and anti-Ran antibody-sensitive process. Green fluorescent protein-metallothionein (GFP-MT) fusion protein was also localized in the nucleus in the stable transformant of CHL-IU cells. These results strongly suggest that the targeting by MT of the nuclear pore is mediated by cytosolic factor(s) other than importins and that MT requires Ran for its nuclear localization.

6/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12189894 BIOSIS NO.: 199900484743
Human monocyte derived dendritic cells express functional P2X and P2Y receptors as well as ecto-nucleotidases.
AUTHOR: Berchtold Susanne; Ogilvie Alexandra L J(a); Bogdan Cornelia; Muehl-Zuerbes Petra; Ogilvie Adaling; Schuler Gerold; Steinkasserer Alexander
AUTHOR ADDRESS: (a)Department of Dermatology, University of Erlangen, Hartmannstr. 14, D-91052, Erlangen**Germany
JOURNAL: FEBS Letters 458 (3):p424-428 Sept. 24, 1999
ISSN: 0014-5793
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: We investigated the expression and function of P2 receptors and ecto-nucleotidases on human monocyte derived **dendritic** cells (DC). In **addition** we analyzed the effect of extracellular **ATP** on the maturation of DC. By RT-PCR, DC were found to express mRNA for several P2X (P2X1, P2X4, P2X5, P2X7) and P2Y (P2Y1, P2Y2, P2Y4, P2Y5, P2Y6, P2Y10, P2Y11) receptors. As shown by FURA-2 measurement, triggering of P2 receptors resulted in an increase in free intracellular Ca2+. In combination with Tumor necrosis factor-alpha, ATP increased the expression of the DC surface markers CD80, CD83 and CD86 indicating a maturation promoting effect. DC expressed the ecto-apyrase CD39 and the ecto-5'-nucleotidase CD73 as demonstrated by RT-PCR. Extracellular ATP was rapidly hydrolyzed by these ecto-enzymes as shown by separation of

3H-labeled ATP metabolites using a thin layer technique. These data suggest that ATP acts as a costimulatory factor on DC maturation.

6/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11876969 BIOSIS NO.: 199900123078
Evidence for heat shock protein immunity in a rat cardiac allograft model of chronic rejection.
AUTHOR: Duquesnoy Rene J(a); Liu Kaihong; Fu Xiao-Fei; Murase Noriko; Ye Qing; Demetris Anthony J
AUTHOR ADDRESS: (a)Div. Transplantation Pathol., Univ. Pittsburgh Med. Cent., Biomedical Sci. Tower Room W1552, Pit**USA
JOURNAL: Transplantation (Baltimore) 67 (1):p156-164 Jan. 15, 1999
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background. The stress response to injury concept has been proposed as a mechanism of chronic rejection. This hypothesis has been tested with a rat cardiac allograft model in recipients pretreated with donor bone marrow (BM) cells. Chronic rejection is manifested in this BM group by obliterative arteriopathy and the epicardium and endocardium contains lymphocytic infiltrates resembling Quilty lesions. Pretreatment with a liver allograft (the orthotopic liver transplant (OLTx) group) is associated with an absence of chronic rejection in the transplanted heart. Methods and Results. Stress responses in the allograft were assessed by determining heat shock protein (hsp) expression by immunohistology of graft tissues and immunoblot analysis of stromal tissue lysates with monoclonal antibodies (mAb) to mammalian hsp60, the inducible hsp72, the constitutively expressed hsc73, and the grp78 C-terminal sequence KSEKDEL (grp78seq). Immunostaining showed clusters of grp78seq-positive cells in the inflammatory infiltrates of obliterated blood vessels and Quilty lesions in the BM group of cardiac allografts. Such grp78seq-positive cells were not seen in the OLTx group of heart allografts nor in syngrafts. Neither group showed significantly different graft myocyte staining of grp78 or hsp72, whereas hsp60 and hsc73 showed higher expression in the BM group and, to a lesser extent, the OLTx group. The increased expression of hsc73 was seen especially in the obliterated arteries and in myocytes nearby cellular infiltrates. Immunoblot analysis of graft stromal tissue lysates showed additional bands with mAb to hsp60 and hsc73 for the OLTx and especially the BM group. No significant bands were seen for hsp72 and grp78. Lymphocytes isolated from chronically rejecting allografts reacted with irradiated autologous spleen cells in the presence of mycobacterial hsp65 and interleukin-2. **Culturing** of graft-infiltrating cells with myocyte clones without alloreactivity, but with strong cobacterial hsp71 and interleukin-2 yielded lymphocyte clones without alloreactivity, but with strong proliferative responsiveness to self-**antigen-presenting** cells and, only in the presence of mycobacterial hsp71 or murine grp78. This T-cell reactivity seemed to require intact hsp molecules because treatment of hsp71 with proteolytic enzymes, polymyxin, or **ATP** abrogated this induction of the **stimulatory** effect of self-**antigen-presenting** cells. These T cells are similar to the hsp-dependent, autoreactive lymphocytes cloned from acutely rejecting rat allografts. Conclusions. These findings support the concept that the pathogenesis of chronic rejection involves a stress response and the participation of graft-infiltrating autoreactive T cells that operate under hsp-dependent mechanisms.

histocompatibility complex class II-negative dendritic cell (DC) precursors that then mature into efficient antigen-presenting cells (APC). To characterize these DC progenitors better, we generated myeloid cell lines from fetal mouse skin by infecting cell suspensions with a retroviral vector carrying an env-AKR-myc-MH2 fusion gene. These cells, represented by the line FSDC, displayed a **dendritic** morphology and their proliferation in serum-free medium was promoted by granulocyte/macrophage colony-**stimulating** factor (GM-CSF), but not macrophage-CSF. FSDC expressed strong surface-membrane **ATP**/ADPase activity, intracellular staining for 2A1 antigen, and a surface phenotype consistent with a myeloid precursor: H-2-d,b+, I-A-d.b+, CD54+, CD11b+, CD11c+, 2.4G2+, F4/80+, CD44+, 2F8+, ERMP 12-, Sca-1+, Sca-2+, NLDC-145-, B7.2+, B7.1-, J11d-, B220-, Thy-1-, and CD3-. FSDC stimulated poorly allogeneic or syngeneic T cells in the primary mixed-leukocyte reaction, and markedly increased this function after treatment with GM-CSF, GM-CSF and interleukin (IL)-4 or interferon-gamma (IFN-gamma); in contrast, stem cell factor, IL-1-alpha and tumor necrosis factor-alpha had no effect. Preculture with IFN-gamma was required for presentation of haptens to primed T cells in vitro. However, FSDC, even after cytokine activation, were less potent APC than adult epidermal Langerhans cells in both of the above assays. Finally, FSDC derivatized with haptens and injected either intravenously or subcutaneously could efficiently induce contact sensitivity responses in naive syngeneic mice. The results indicate that fetal mouse skin is colonized by myeloid precursors possessing a macrophage/immature DC-like surface phenotype and priming capacity in vivo. These cells need further differentiation and activation signals (e.g. cytokines) to express their antigen presenting potential in vitro.

6/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09868766 BIOSIS NO.: 199598323684
Role of extracellular adenosine triphosphate in the cytotoxic T-lymphocyte-mediated lysis of antigen presenting cells.
AUTHOR: Blanchard D Kay; Wei Sheng(a); Duan Chunni; Pericle Federica; Diaz Jose I; Djeu Julie Y
AUTHOR ADDRESS: (a)H. Lee Moffitt Cancer Cent. Res. Inst., 12902 Magnolia Dr., Tampa, FL 33612**USA
JOURNAL: Blood 85 (11):p3173-3182 1995
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The lysis of antigen presenting cells (APCs) by cytotoxic T lymphocytes (CTLs) may be one mechanism whereby an immune response is downregulated by Staphylococcus superantigens. Disappearance of monocytes/macrophages from staphylococcal enterotoxin A (SEA)-activated peripheral blood mononuclear cell (PBMC) cultures, but not from control PBMC cultures was seen by flow cytometry. Recently, adenosine triphosphate (ATP) has been described as an effector molecule in CTL-mediated lysis of some murine tumor target cells. We have also shown that ATP caused the lysis of human macrophages, and that treatment of cells with interferon gamma (IFN-gamma) rendered macrophages significantly more sensitive to ATP than untreated cells. To show that this purine nucleotide may play a role in modulating the immune system, we generated human CTLs that were stimulated with SEA, and used them as effector cells against SEA-pulsed autologous macrophages. CTLs were found to specifically lyse SEA-pulsed macrophages, while control, unpulsed, macrophages were unaffected. The addition of hexokinase, an enzyme that hydrolyzes ATP, significantly abrogated the killing of SEA-pulsed cells during the assay. In examining the mechanism of cytotoxicity, electron

microscopy showed that macrophages **incubated** with both **ATP** and CTLs underwent necrosis, rather than apoptosis. From these results, it is suggested that **ATP** is released from CTLs during **antigen presentation**, and that IFN-gamma-activated macrophages, which are inherently more sensitive to this mediator, are readily lysed and therefore removed from circulation, thus downregulating an immune response.

6/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09712304 BIOSIS NO.: 199598167222
Morphologic and ultrastructural evidence for interleukin-6 induced platelet activation.
AUTHOR: Oleksowicz Leslie(a); Mrowiec Zbigniew; Isaacs Randi; Dutcher Janice P; Puszkin Elena
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JOURNAL: American Journal of Hematology 48 (2):p92-99 1995
ISSN: 0361-8609
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The in vitro effect of IL-6 on platelet activation was investigated. When human platelets were incubated with high (1,000 ng/ml) or low (1 ng/ml) dose IL-6, expression of GMP-140 was enhanced by 42% (N = 6; P lt 0.009) and 46% (N = 6; P lt 0.061) in 1 hr low and high dose IL-6-platelet incubations, respectively, as assessed by flow cytometry. In platelet specimens incubated with high dose IL-6 for 3 hr, a 70% (N = 6; P lt 0.009) increase in GMP-140 expression over control was observed. Parallel high dose IL-6 incubations subjected to scanning electron microscopic studies revealed a 3.4-fold increase (N = 6; P lt 0.001) in spheroid morphologic platelet forms in 1 hr **incubations** in comparison to control platelet preparations, whereas in 3 hr IL-6-platelet **incubations**, a 96% increase in **dendritic** platelet forms was observed (N = 6; P lt 0.001). Significant increases in platelet **ATP** levels were observed in both I min and 1 hr high dose and low dose IL-6 platelet incubations. In 3 hr high dose-IL-6 platelet incubations, a significant 18% (N = 8; P lt 0.001) decrease in platelet ATP was paralleled by a significant 40% increase (N = 8; P lt 0.014) in plasma ATP in the same specimens. This increased plasma ATP was highly correlated with a reduction in platelet ATP when analyzed by bivariate regression analysis. Lastly, transmission electron microscopic analysis demonstrated a significant reduction in dense granule number and ratio of dense granule surface area/cell surface area in 3 hr high dose IL-6 incubations. These findings suggests that IL-6 activates platelets in vitro.

6/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09223185 BIOSIS NO.: 199497231555
Contraction of the guinea pig isolated, perfused trachea to purine and pyrimidine agonists.
AUTHOR: Fedan Jeffrey S(a); Stem Jeese L; Day Brian
AUTHOR ADDRESS: (a)Physiol. Sect., Natl. Inst. Occupational Safety Health, 944 Chestnut Ridge Rd., Morgantown, WV 2**USA
JOURNAL: Journal of Pharmacology and Experimental Therapeutics 268 (3):p 1321-1327 1994

ISSN: 0022-3565
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Unlike methacholine and histamine, ATP and uridine 5'-triphosphate (UTP) are more potent contractile agonists when they are applied to the mucosal (intraluminal, IL) surface of the guinea pig perfused trachea than when they are applied to the serosal (extraluminal, EL) surface. The relative contractile activities of a series of purine and pyrimidine compounds were assessed. The order of EL activity was: (2-methylthio ATP (2 MeSATP) = adenosine 5'-diphosphate (ADP)) gt (adenosine 5'-O-(2-thiodiphosphate) (ADP-beta-S) = ATP = adenosine 5'-O-(3-thiotriphosphate) (ATP-gamma-S)) gt ((beta,gamma-imido ATP) (APPNP) = alpha,beta-methylene ATP (APCPP)) gt (UTP = uridine 5'-diphosphate (UDP) = inosine 5'-triphosphate (ITP)) gt (xanthosine 5'-triphosphate (XTP) beta,gamma-methylene ATP (APPCP)). EL adenosine, adenosine 5'-monophosphate, uridine 5'-monophosphate and uridine were weak or inactive. The EL-order of activity, therefore, shares some characteristics of P-2Y receptors. The order of IL activity was: (**ATP** = UTP = ITP) gt (**ATP**-gamma-S = ADP = APPNP = 2 MeSATP) gt (UDP = ADP-beta-S = XTP) gt **APCPP**; the other compounds were weak or inactive. The IL order of activity, therefore, resembled that for P-2U or "nucleotide receptors." **ATP**, APPNP, UTP, UDP, ITP and XTP were more active when **added** to the IL than after administration to the EL bath; the remaining compounds were similarly active EL and IL, or were more active EL than IL. Greater IL than EL activity of agonists was a property associated with preference for P-2U-receptors. The EL and IL activities of the agonists compare favorably with those reported for basolateral and apical stimulation of short circuit current and (Ca++)-i of human respiratory epithelium, and phospholipase C activation of cultured human airway epithelium.

6/7/15 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08133035 BIOSIS NO.: 000093120183
P-2-PURINOCEPTOR ACTIVATION STIMULATES PHOSPHOINOSITIDE HYDROLYSIS AND INHIBITS ACCUMULATION OF CAMP IN CULTURED VENTRICULAR MYOCYTES
AUTHOR: YAMADA M; HAMAMORI Y; AKITA H; YOKOYAMA M
AUTHOR ADDRESS: FIRST DEP. INTERNAL MEDICINE, KOBE UNIVERSITY SCHOOL MEDICINE, 5-1 KUSUNOKI-CHO, 7-CHOME, CHUO-KU, KOBE 650, JPN.
JOURNAL: CIRC RES 70 (3). 1992. 477-485. 1992
FULL JOURNAL NAME: Circulation Research
CODEN: CIRUA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Extracellular ATP modulates cardiac contraction through P2-purinoceptors on cardiac myocytes. To elucidate the molecular mechanism of this response, we examined the effects of P2-purinoceptor activation on phosphoinositide (PI) hydrolysis and the cAMP system in cultured ventricular myocytes of fetal mice. In a concentration-dependent manner, ATP stimulated accumulations of [3H]inositol monophosphate, bisphosphate, and trisphosphate with the half-maximum effective concentration of .apprx.1 .mu.M in the myocytes labeled with [3H]inositol. The order of efficacy of a series of adenyl compounds for **stimulation** of PI hydrolysis was adenosine 5'-O-(3-thiotriphosphate) (**ATP**.gamma.S), **ATP** > ADP, 5'-adenylylimidodiphosphate (APPNP) > .alpha.,.beta.-methyleneadenosine 5'-triphosphate (**APCPP**) > .beta.,.gamma.-methyleneadenosine 5'-triphosphate, AMP > adenosine. On the other hand, 100 .mu.M **ATP**

.gamma.S inhibited isoproterenol-induced accumulation of cAMP by .apprx.70% without decreasing the time to maximal cAMP levels, as measured by radioimmunoassay. This response was also concentration dependent, with a half-maximum inhibitory concentration (IC50) of .apprx.1 .mu.M. All of the tested ATP, ADP, and ATP analogues inhibited the cAMP system, and the responses to ATP.gamma.S, APPNP, and APCPP were insensitive to an A1-purinoceptor antagonist, 8-cyclopentyl-1,3-dipropylxanthine. Pertussis toxin attenuated the ATP-induced PI hydrolysis by no more than 25% at 100 ng/ml but completely suppressed the ATP.gamma.S-induced inhibition of the cAMP system. Protein kinase C-activating phorbol ester, 4.beta.-phorbol 12.beta.-myristate 13.alpha.-acetate, inhibited the ATP-induced PI hydrolysis with an IC50 of .apprx.1 nM and also attenuated the ATP.gamma.S-induced inhibition of the cAMP system at .gtoreq. 1 nM, although a biologically inactive phorbol ester, 4.alpha.-phorbol 12,13-didecanoate, did not. From these data, P2-purinoceptor activation stimulates PI hydrolysis by activating phospholipase C primarily through pertussis toxin-insensitive G proteins and attenutes cAMP accumulation by inhibiting adenylate cyclase through pertussis toxin-sensitive G proteins. Protein kinase C is likely to negatively regulate both the signal transduction systems.

6/7/16 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08039885 BIOSIS NO.: 000093073233
INCREASED ANTIPLATELET T HELPER LYMPHOCYTE REACTIVITY IN PATIENTS WITH AUTOIMMUNE THROMBOCYTOPENIA
AUTHOR: SEMPLE J W; FREEDMAN J
AUTHOR ADDRESS: DEP. IMMUNOHEMATOLOGY, ST. MICHAEL'S HOSP., 30 BOND ST., TORONTO ONTARIO M5B 1W8, CANADA.
JOURNAL: BLOOD 78 (10). 1991. 2619-2625. 1991
FULL JOURNAL NAME: Blood
CODEN: BLOOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Chronic autoimmune thrombocytopenic purpura (ATP) is an common hematologic disorder in which platelet-specific autoantibodies bind to platelets and enhance their destruction by the reticuloendothelial system. While there has been considerable investigation of the hmoral immune abnormalities in ATP, little work has been performed on the cellular immunoregulatory aspects of this autoimmune disorder. We describe here that patients with **ATP** have lymphocytes that proliferate normally when **stimulated** by mitogens. However, when **stimulated** by normal control platelets in 7-day **antigen-presenting** cell **cultures**, peripheral blood mononuclear cells (PBMC) from patients with **ATP** proliferate at significantly higher levels (P < .001) and their lymphocytes secrete significantly higher amounts of interleukin-2 (IL-2) (P < .001) than do lymphocytes from control subjects. Depletion studies with monoclonal anti-CD8 and complement did not reduce the proliferative capacity of the responding PBMC population, indicating that CD4+ T-helper cells may be responsible for the response. Phenotypic analysis of peripheral blood lymphocyte subsets from patients with ATP showed that there was a significant reduction in CD4+ Leu8+ T suppressor-inducer cells (P < .001) and a concomitant increase in CD3+DR+ activated T cells (P < .001) and CD19+ B cells (P < .05). These data indicate that CD4+ T-helper cells from patients with ATP are stimulated by normal platelet antigen(s) to secrete IL-2 and may modulate the enhanced antiplatelet autoantibody response.

6/7/17 (Item 17 from file: 5)

DIALOG(R)File 5:Biosis Previews(R)

07868269 BIOSIS NO.: 000092127635
LOCALIZATION OF ATPASE ACTIVITY IN DENDRITIC SPINES OF THE CEREBRAL CORTEX
AUTHOR: COHEN R S; KRIHO V
AUTHOR ADDRESS: DEP. ANATOMY CELL BIOL., UNIVERSITY ILLINOIS AT CHICAGO, 808 SOUTH WOOD STREET, CHICAGO, ILL. 60612.
JOURNAL: J NEUROCYTOL 20 (9). 1991. 703-715. 1991
FULL JOURNAL NAME: Journal of Neurocytology
CODEN: JNCYA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: An ATPase activity has been demonstrated in **dendritic** spines of the adult rat cerebral cortex using cerium to capture inorganic phosphate that is liberated during the enzymatic hydrolysis of **ATP**. Small pieces of cerebral cortex were fixed and **incubated** in a standard incubation medium containing both Ca2+ and Mg2+ at pH 7.2; other modifications of the incubation medium are described below. Electon microscopic examination of the cerium phosphate reaction product showed an electron dense precipitate localized in the cytoplasm of the spine behind the postsynaptic density. Whereas the postsynaptic density, itself, is not reactive, dense reaction product is seen immediately underneath the postsynaptic density and extending into the subsynaptic web. Reaction product is also associated with membranous cisternae within the dendritic spine. The reaction occurred in the presence of Ca2+ and Mg2+ and either of these two ions alone. However, virtually no reaction product is seen when the tissue was incubated in medium devoid of Ca2+ and Mg2+, or in a medium containing Mg2+ and EGTA, suggesting that trace Ca2+ is necessary, but not sufficient for the reaction. Addition of p-chloromercurobenzoate, which selectively blocks SH groups, inhibited the reaction in the presence of Ca2+ and Mg2+, or both of these ions. The effect of pH on the reaction was determined using a lead precipitation method. The reaction occurred at pH 9.2 in the presence of Ca2+ alone. In the presence of Mg2+ alone, the reaction product appeared somewhat reduced at this pH. The presence of an ATPase activity, which is dependent upon Ca2+ in dendritic spines where actin and actin-binding proteins have also been localized, suggests that this activity may be involved in the dynamics of cytoskeletal function leading to shape changes in dendritic spines and synapses, as seen with various physiological and behavioral paradigms.

6/7/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07517765 BIOSIS NO.: 000091080894
EXPOSURE OF THIOL GROUPS AND BOUND NUCLEOTIDE IN G ACTIN THIOLS AS AN INDICATOR FOR THE NATIVE STATE OF ACTIN
AUTHOR: STOURNARAS C
AUTHOR ADDRESS: DEP. BASIC SCI., SCH. MED., UNIVERSITY CRETE, GR-714 09 IRALION, GREECE.
JOURNAL: ANTICANCER RES 10 (6). 1990. 1651-1660. 1990
FULL JOURNAL NAME: Anticancer Research
CODEN: ANTRD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In monomeric actin the number of thiol groups exposed to thiol reagents and the nucleotide bound are found to be correlated. G-actin, prepared as normally in the presence of ATP, exposed one thiol group (nSH = 1). In the presence of 1 equivalent ADP, as found associated with

G-actin preparations when no nucleotide is added, the protein exposed four thiol groups (nSH = 4). When G-actin was prepared in a high excess of ADP (50 eq.) two thiol groups became exposed (nSH = 2). Actin also exposed four thiol groups when depolymerized in buffers containing 10 eq. APCPP or APPCP, with a time course of the thiol-titration similar to that obtained when the protein was prepared in a nucleotide-free buffer. When actin was depolymerized in a buffer containing 10 eq. APPNP it also exposed 4 thiols; however, titration kinetics are different. In this case, one thiol group reacted quickly, while the reaction of the three others was retarded. Finally, when actin was depolymerized in the ADP-analog **APCP** it also exposed four thiol groups, with titration kinetics similar to those obtained for actin in nucleotide free buffer. It was concluded that **addition** of **ATP** induced a shielding effect on three out of four thiol groups in monomeric actin. ADP (50 eq.) shielded two of the four thiol groups, while ATP- and ADP-analogs had no shielding effect. The thiol shielding activity and the protective capacity of a nucleotide are interrelated. Actin preparations, in ATP or ADP (high excess) containing buffers, with one or two thiol groups exposed respectively, are stable and polymerizable over many hours. Actin prepared in buffers containing ATP- or ADP-analogs, exposing four thiol groups, is denatured, losing its capacity to polymerize within a few hours. Finally, actin preparations in nucleotide free buffers, with four thiol groups exposed, are rapidly denatured, losing the capacity to polymerize within less than one hour. Thus denaturation of monomeric actin must be understood in terms of loss of thiol shielding. In actin preparations generally the ability to polymerize was lost when, even after addition of ATP to solutions of G-actin, the number of thiol groups exposed was greater than two. It was concluded that in monomeric actin changes in the accessibility of thiol groups, loss of nucleotide binding capacity as well as loss of the polymerization capability of the protein are events which probably represent different aspects of the denaturation process in G-actin. Thus the number of titratable thiol groups (nSH) is proposed to be an indirect indicator of actin nativeness and conformation.

6/7/19 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07031315 BIOSIS NO.: 000089112864
ADENINE NUCLEOTIDES MODULATE PHOSPHATIDYLCHOLINE METABOLISM IN AORTIC ENDOTHELIAL CELLS
AUTHOR: PIROTTON S; ROBAYE B; LAGNEAU C; BOEYNAEMS J-M
AUTHOR ADDRESS: INST. INTERDISCIPLINARY RES., SCH. MED., FREE UNIV. BRUSSELS, CAMPUS ERASME, BRUSSELS, BELGIUM.
JOURNAL: J CELL PHYSIOL 142 (3). 1990. 449-457. 1990
FULL JOURNAL NAME: Journal of Cellular Physiology
CODEN: JCLLA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: ATP and ADP, in concentrations ranging from 1-100 .mu.M, increased the release of [3H]choline and [3H]phosphorylcholine (P-choline) from bovine aortic endothelial cells (BAEC) prelabelled with [3H]choline. This action was detectable within 5 minutes and was maintained for at least 40 minutes. ATP and ADP were equiactive, and their action was mimicked by their phosphorothioate analogs (**ATP** .gamma.S and ADP.beta.S) and adenosine 5'-(.beta.,.gamma. imido) triphosphate (APPNP), but not by AMP, adenosine, and adenosine 5'-(.alpha.,.beta. methylene)triphosphate (**APCPP**): these results are consistent with the involvement of P2.gamma. receptors. **ATP** also induced an intracellular accumulation of [3H]choline: the intracellular levels of [3H]choline was increased 30 seconds after

ATP addition and remained elevated for a least 20 minutes. The action of ATP on the release of choline metabolites was reproduced by bradykinin (1 .mu.M), the tumor promoter phorbol 12-myristate 13-acetate (PMA, 50 nM), and the calcium ionophore A23187 (0.5 .mu.M). Down regulation of protein kianse C, following a 24-hour exposure of endothelial cells to PMA, abolished the effects of PMA and ATP on the release of choline and P-choline, whereas the response to A23187 was maintained. These results suggest that in aortic endothelial cells, ATP produces a sustained activation of a phospholipase D hydrolyzing phosphatidylcholine. The resulting accumulation of phosphatidic acid might have an important role in the modulation of endothelial cell function by adenine nucleotides. Stimulation of phospholipase D appears to involve protein kinase C, activated following the release of diacylglycerol from phosphatidylinositol bisphosphate by a phospholipase C coupled to the p2.gamma. receptors.

6/7/20 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06862643 BIOSIS NO.: 000089012233
DIFFERENTIAL BLOCKADE OF AGONIST AND DEPOLARIZATION-INDUCED CALCIUM-45 INFLUX IN SMOOTH MUSCLE CELLS
AUTHOR: WALLNOFER A; CAUVIN C; LATEGAN T W; RUEGG U T
AUTHOR ADDRESS: PRECLINICAL RES., 386/422, SANDOZ LTD., CH-4002 BASEL, SWITZERLAND.
JOURNAL: AM J PHYSIOL 257 (4 PART 1). 1989. C607-C611. 1989
FULL JOURNAL NAME: American Journal of Physiology
CODEN: AJPHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: ATP stimulated 45Ca2+ influx in rat aortic smooth muscle cells in a concentration-dependent manner (EC50 = 3.6 .+-. 0.5 .times. 10-7 M). ADP and GTP were less effective than ATP in **stimulating** 45Ca2+ influx; AMP was weakly active and the adenosine agonist 5'-(N-ethyl-carboxamido)-adenosine (NECA) had no effect. **ATP** .gamma.S was about equieffective with **ATP**, whereas .alpha.,.beta.-methylene-**ATP** (**APCPP**) did not induce 45Ca2+ influx. **Stimulation** of 45Ca2+ influx by **ATP** was not abolished by the dihydropyridine Ca2+ channel antagonist darodipine (PY 108-068), which completely blocked depolarization-induced 45Ca2+ influx. Inorganic cations (La3+, Cd2+, Co2+, Ni2+, Mn2+, and Mg2+) were able to inhibit both agonist- and depolarization-induced 45Ca2+ influx. Cd2+, however, was .apprx. 20 times more selective in blocking K+-stimulated than agonist-stimulated 45Ca2+ influx. These data indicate that ATP-stimulated Ca2+ influx in rat aortic smooth muscle cells is resistant to darodipine but is reduced by La3+, Cd2+, and other inorganic blockers of Ca2+ channels.

6/7/21 (Item 21 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06845425 BIOSIS NO.: 000089004617
CULTURED HUMAN LANGERHANS CELLS RESEMBLE LYMPHOID DENDRITIC CELLS IN PHENOTYPE AND FUNCTION
AUTHOR: ROMANI N; LENZ A; GLASSEL H; STOESSEL H; STANZL U; MAJDIC O; FRITSCH P; SCHULER G
AUTHOR ADDRESS: DEP. DERMATOL., UNIV. INNSBRUCK, A-6020 INNSBRUCK, AUSTRIA.
JOURNAL: J INVEST DERMATOL 93 (5). 1989. 600-609. 1989
FULL JOURNAL NAME: Journal of Investigative Dermatology

CODEN: JIDEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Freshly isolated murine epidermal Langerhans cells (LC) are weak stimulators of resting T cells. Upon culture their phenotype changes, their stimulatory activity increases significantly, and they come to resemble lymphoid dendritic cells. Resident murine LC, therefore, might represent a reservoir of immature dendritic cells. We have now used enzyme cytochemistry, a panel of some 80 monoclonal antibodies, and immunofluorescence microscopy or two-color flow cytometry, as well as transmission electron microscopy, to analyse the phenotype and morphology of human LC before and after 2-4 d of bulk epidermal cell culture. In **addition**, LC were enriched from bulk epidermal cell **cultures**, and their **stimulatory** capacity was tested in the allogeneic mixed leukocyte reaction and the oxidative mitogenesis assay. **Cultured** human LC resembled human lymphoid **dendritic** cells in morphology, phenotype, and function. Specifically, LC became non-adherent upon **culture** and developed sheet-like processes (so-called "veils"), decreased their surface **ATP**/ADP'ase activity, and lost nonspecific esterase activity. As in the mouse, surface expression of MHC class I and II antigens increased significantly, and FcII receptors were significantly reduced. Markers that are expressed by dendritic cells (like CD40) appeared on LC following culture. Cultured human LC were potent T-cell stimulators. Our findings support the view that resident human LC, like murine LC, represent immature precursors of lymphoid dendritic cells in skin-draining lymph nodes.

6/7/22 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06582184 BIOSIS NO.: 000087024345
STIMULATION OF PROSTACYCLIN RELEASE FROM AORTIC SMOOTH MUSCLE CELLS BY PURINE AND PYRIMIDINE NUCLEOTIDES
AUTHOR: DEMOLLE D; LAGNEAU C; BOEYNAEMS J-M
AUTHOR ADDRESS: I.R.I.B.H.N., CAMPUS ERASME, BLDG. C, ROUTE DE LENNIK 808, B-1070 BRUSSELS, BELG.
JOURNAL: EUR J PHARMACOL 155 (3). 1988. 339-344. 1988
FULL JOURNAL NAME: European Journal of Pharmacology
CODEN: EJPHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: ATP and ATP.gamma.S(10-100 .mu.M) stimulated the release of prostacyclin (PGI2) from bovine aortic smooth muscle cells. This effect was reproduced by UTP, ITP and partially by GTP. ADP and ADP.beta.S, the P2X-selective agonist .alpha.,.beta.-methylene **ATP** (**APCPP**), AMP and adenosine were all inactive. This effect of **ATP**.gamma.S was not inhibited by Reactive Blue 2, an antagonist of P2Y receptors. The **stimulation** of PGI2 production in aortic smooth muscle cells by these nucleotides thus seems to involve receptors distinct from both P2X and P2Y subtypes, which are responsible for smooth muscle contraction and PGI2 release from endothelial cells, respectively.

6/7/23 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05734537 BIOSIS NO.: 000084082943
A DOPAMINERGIC CELL LINE VARIANT RESISTANT TO THE NEUROTOXIN 1 METHYL-4-PHENYL-1 2 3 6-TETRAHYDROPYRIDINE

AUTHOR: DENTON T; HOWARD B D
AUTHOR ADDRESS: DEP. BIOLOGICAL CHEM., UCLA SCH. MED., LOS ANGELES, CALIF. 90024.
JOURNAL: J NEUROCHEM 49 (2). 1987. 622-630. 1987
FULL JOURNAL NAME: Journal of Neurochemistry
CODEN: JONRA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: 1-Methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) is known to cause parkinsonism by killing dopaminergic neurons; the toxic substance is a metabolite, 1-methyl-4-phenylpyridinium ion (MPP+). PC12 cells, which are dopaminergic are killed in culture by MPTP and MPP+ but at concentrations much higher than that required to kill affected neurons in vivo. However, at low concentrations (10-100 .mu.M), MPP+ caused an increased production of lactate by PC12 cells. MPP+-treated PC12 cels exhibited decreased mitochondrial respiration. Mitochondria from the treated cells respired normally in the presence of added succinate but not .beta.-hydroxybutyrate, a finding indicating that MPP+ inhibits the oxidation of some substrates selectively. MPP+ was more effective in killing the cells when glycolysis was reduced with 2-deoxyglucose or by lowering the glucose content of the **culture** medium. Under these conditions, MPP+ inhibited **ATP** synthesis and depleted cellular stores of **ATP**. **APC12** variant that is even more resistant to MPTP and MPP+ than are wild-type cells had been isolated. The MPTP-resistant variant is also more resistant to the lethal effects of oligomycin, antimycin A, and rotenone. Ths variant exhibited altered lactate production and mitochondrial respiration. It is suggested that some brain neurons that accumulate MPP+ without being kililed by it may also have an energy metabolism somewhat different from that of more sensitive neurons.

6/7/24 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

04257199 BIOSIS NO.: 000077083244
DI NUCLEOTIDE PRIMERS FACILITATE CONVENIENT IDENTIFICATION OF THE MOUSE RIBOSOMAL DNA TRANSCRIPTION INITIATION SITE A GENERAL METHOD FOR ANALYSIS OF TRANSCRIPTION BY RNA POLYMERASES I AND III
AUTHOR: WILKINSON J A K; MILLER K G; SOLLNER-WEBB B
AUTHOR ADDRESS: JOHNS HOPKINS UNIV., SCH. MED., BALTIMORE, MD. 21205.
JOURNAL: J BIOL CHEM 258 (22). 1983. 13919-13928. 1983
FULL JOURNAL NAME: Journal of Biological Chemistry
CODEN: JBCHA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The in vitro initiation site for RNA polymerase I on the mouse rRNA gene was identified using a new method that is generally applicable to the study of other eukaryotic transcripts. First, the 5' end of mouse rRNA was located to an ApC... by high resolution S1 nuclease mapping. Dinucleotide primers were then used in transcription reactions to demonstrate that this position is the actual de novo initiation site, and not a rapid RNA processing site. For this analysis, initiation was inhibited by reduced rXTP [ribonucleoside triphosphate] concentration, and, upon supplementation with various dinucleotides, only **ApC stimulated** correct synthesis. Independently confirming its role as the initiating nucleotide, **ATP** was shown to be required at a much higher concentration than the other rXTP for RNA initiation, but not for elongation. These results also demonstrate a marked sequence conservation of rRNA initiation sites between the mouse and frog, 2 spp. that violate the general rule of species specificity in RNA polymerase I initiation.

Extending these studies to RNA polymerase III, the initiation site for 5S RNA can be similarly located by dinucleotide analysis and confirmed from the concentration requirements of each rXTP. In addition to allowing initiation at suboptimal rXTP concentration, dinucleotide primers can also circumvent the need for a factor normally required for initiation, suggesting their potential value in dissecting the mechanism of eukaryotic transcription.

6/7/25 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

10946329 EMBASE No: 2000436626
The P2 purinergic receptors of human dendritic cells: Identification and coupling to cytokine release
Ferrari D.; La Sala A.; Chiozzi P.; Morelli A.; Falzoni S.; Girolomoni G.; Idzko M.; Dichmann S.; Norgauer J.; Di Virgilio F.
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FASEB Journal (FASEB J.) (United States) 2000, 14/15 (2466-2476)
CODEN: FAJOE ISSN: 0892-6638
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 54

We investigated the expression of purinoceptors in human dendritic cells, providing functional, pharmacological, and biochemical evidence that immature and mature cells express P2Y and P2X subtypes, coupled to increase in the intracellular Casup 2sup +, membrane depolarization, and secretion of inflammatory cytokines. The ATP-activated Casup 2sup + change was biphasic, with a fast release from intracellular stores and a delayed influx across the plasma membrane. A prolonged exposure to ATP was toxic to dendritic cells that swelled, lost typical dendrites, became phase lucent, detached from the substrate, and eventually died. These changes were highly suggestive of expression of the cytotoxic receptor P2Xinf 7, as confirmed by ability of dendritic cells to become permeant to membrane impermeant dyes such as Lucifer yellow or ethidium bromide. The P2Xinf 7 receptor ligand 2',3'-(4-benzoylbenzoyl)-ATP was a better agonist then ATP for Casup 2sup + increase and plasma membrane depolarization. Oxidized ATP, a covalent blocker of P2X receptors, and the selective P2Xinf 7, antagonist KN-62 inhibited both permeabilization and Casup 2sup + changes induced by **ATP**. The following purinoceptors were expressed by immature and mature **dendritic** cells: P2Yinf 1, P2Yinf 2, P2Yinf 5, P2Yinf 1inf 1 and P2Xinf 1, P2Xinf 4, P2Xinf 7. Finally, **stimulation** of LPS-matured cells with **ATP** triggered release of IL-1beta and TNF-alpha. Purinoceptors may provide a new avenue to modulation of **dendritic** cells function.

6/7/26 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

05575720 EMBASE No: 1993343820
Standing calcium gradients in olfactory receptor neurons can be abolished by Amiloride or Ruthenium Red
Lischka F.W.; Schild D.
Physiologisches Institut, Universitat Gottingen, Humboldtallee 23,D-37073 Gottingen Germany
Journal of General Physiology (J. GEN. PHYSIOL.) (United States) 1993, 102/5 (817-831)

CODEN: JGPLA ISSN: 0022-1295
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Digital imaging and the patch clamp technique were used to investigate the intracellular calcium concentration in olfactory receptor neurons using the Casup 2sup + indicator dyes fura-2 and fura-2/AM. The spatial distribution of Ca(i)sup 2sup + as well as its modification by the drugs Amiloride and Ruthenium Red were studied. Resting calcium concentrations in cells loaded with fura- 2/AM were between 10 and 200 nM. In cells that were loaded with the pentapotassium salt of fura-2 through the patch pipette, calcium concentrations were in the same range if **ATP** was **added** to the pipette solution. Otherwise, Casup 2sup + reached concentrations of ~ 500 nM. Most of the observed cells showed a standing gradient of calcium, the calcium concentrations in the distal **dendritic** end of the cell being higher than in the soma. In some cells, the gradient was markedly reduced or abolished by adding either Amiloride or Ruthenium Red to the bath solution. In a few cells, neither drug had any effect upon the gradient. It is suggested that the inhomogenous spatial distribution of intracellular calcium in olfactory cells of Xenopus laevis is brought about by an influx of calcium ions through two different calcium permeable conductances in the peripheral compartments of the cells. The fact that only either Ruthenium Red or Amiloride abolished the standing calcium gradient further suggested that the two conductances blocked were presumably not coexpressed in the same cells.

6/7/27 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

05113695 EMBASE No: 1992253911
Energetics of defective macrophage antigen presentation after hemorrhage as determined by ultraresolution sup 3sup 1P nuclear magnetic resonance spectrometry: Restoration with adenosine triphosphate-MgClinf 2
Meldrum D.R.; Ayala A.; Chaudry I.H.
Department of Surgery, B424 Clinical Center, Michigan State University,East Lansing, MI 48824-1315 United States
Surgery (SURGERY) (United States) 1992, 112/2 (150-158)
CODEN: SURGA ISSN: 0039-6060
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Background. The purpose of this study was to determine whether a decrease in macrophage energetics contributes to the profound immune dysfunction that occurs after hemorrhage and, if so, whether adenosine triphosphate (ATP)- MgClinf 2 treatment has any beneficial effects on the above parameters. Methods. C3H/HeN mice were bled to a mean blood pressure of 35 mm Hg, maintained at that pressure for 60 minutes, resuscitated with their own shed blood and Ringer's lactate, and treated with ATP-MgClinf 2 (80 mumol/kg body weight) or saline solution (vehicle). Peritoneal macrophages were harvested 1 hour after resuscitation and **ATP** levels were determined by sup 3sup 1P nuclear magnetic resonance spectrometry. In **addition**, macrophage functions were determined by measuring **antigen presentation** capacity (AP), as well as interleukin-1 (IL- 1), interleukin-6 (IL-6), and tumor necrosis factor (TNF) synthesis. Results. Hemorrhage caused a significant decrease in peritoneal macrophage AP function, as well as IL-1, IL-6, and TNF synthesis, by 52% +/- 14%, 91% +/- 12%, 78% +/- 8%, and 89% +/- 8%, respectively, which was correlated with a 78% +/- 6% decrease in macrophage ATP levels ($p < 0.05$). Treatment with ATP-MgClinf 2 after hemorrhage restored macrophage ATP levels ($p < 0.05$) and significantly increased ($p < 0.05$) macrophage AP, IL-1, IL-6, and TNF release by 110% +/- 21%, 130% +/- 38%, 124% +/- 17%, and 66% +/- 24%, respectively. Conclusions. The decreased macrophage ATP levels may be the

cause of defective macrophage AP and cytokine release after hemorrhage, and both macrophage ATP levels and macrophage immune functions can be restored with adjuvant ATP-MgClinf 2 treatment after hemorrhage.

6/7/28 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

04936176 EMBASE No: 1992076392
Pinf 2-purinoceptor activation stimulates phosphoinositide hydrolysis and inhibits accumulation of cAMP in cultured ventricular myocytes
Yamada M.; Hamamori Y.; Akita H.; Yokoyama M.
First Dept. of Internal Med., Kobe University, School of Medicine, 5-1 Kusunoki-cho,Chuo-ku, Kobe 650 Japan
Circulation Research (CIRC. RES.) (United States) 1992, 70/3 (477-485)
CODEN: CIRUA ISSN: 0009-7330
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Extracellular ATP modulates cardiac contraction through Pinf 2-purinoceptors on cardiac myocytes. To elucidate the molecular mechanism of this response, we examined the effects of Pinf 2-purinoceptor activation on phosphoinositide (PI) hydrolysis and the cAMP system in cultured ventricular myocytes of fetal mice. In a concentration-dependent manner, ATP stimulated accumulations of (sup 3H)inositol monophosphate, bisphosphate, and trisphosphate with the half- maximum effective concentration of ~1 muM in the myocytes labeled with (sup 3H)inositol. The order of efficacy of a series of adenyl compounds for **stimulation** of PI hydrolysis was adenosine 5'-O-(3-thiotriphosphate) (ATPgammaS), **ATP**>ADP, 5'-adenylylimidodiphosphate (APPNP)>alpha,beta-methyleneadenosine 5'-triphosphate (**APCPP**)>beta,gamma-methyleneadenosine 5'- triphosphate, AMP>adenosine. On the other hand, 100 muM ATPgammaS inhibited isoproterenol-induced accumulation of cAMP by ~70% without decreasing the time to maximal cAMP levels, as measured by radioimmunoassay. This response was also concentration dependent, with a half-maximum inhibitory concentration (IC$D5inf 0) of ~1 muM. All of the tested ATP, ADP, and ATP analogues inhibited the cAMP system, and the responses to ATPgammaS, APPNP, and APCPP were insensitive to an Ainf 1-purinoceptor antagonist, 8-cyclopentyl-1,3- dipropylxanthine. Pertussis toxin attenuated the ATP-induced PI hydrolysis by no more than 25% at 100 ng/ml but completely suppressed the ATPgammaS-induced inhibition of the cAMP system. Protein kinase C-activating phorbol ester, 4beta-phorbol 12beta-myristate 13alpha-acetate, inhibited the ATP-induced PI hydrolysis with an IC$D5inf 0 of ~1 nM and also attenuated the ATPgammaS-induced inhibition of the cAMP system at >=1 nM, although a biologically inactive phorbol ester, 4alpha-phorbol 12,13-didecanoate, did not. From these data, Pinf 2- purinoceptor activation stimulates PI hydrolysis by activating phospholipase C primarily through pertussis toxin-insensitive G proteins and attenuates cAMP accumulation by inhibiting adenylate cyclase through pertussis toxin- sensitive G proteins. Protein kinase C is likely to negatively regulate both the signal transduction systems.

6/7/29 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

04094337 EMBASE No: 1989263383
Differential blockade of agonist- and depolarization-induced sup 4sup 5Casup 2sup + influx in smooth muscle cells
Wallnofer A.; Cauvin C.; Lategan T.W.; Ruegg U.T.
Preclinical Research, Sandoz Limited, 4002 Basel Switzerland

American Journal of Physiology - Cell Physiology (AM. J. PHYSIOL. CELL PHYSIOL.) (United States) 1989, 257/4 (26/4) (C607-C611)
CODEN: AJPCD ISSN: 0002-9513
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

ATP stimulated sup 4sup 5Casup 2sup + influx in rat aortic smooth muscle cells in a concentration-dependent manner (EC$D5inf 0 = 3.6 +/- 0.5 x 10sup -sup 7 M). ADP and GTP were less effective than ATP in **stimulating** sup 4sup 5Casup 2sup + influx; AMP was weakly active and the adenosine agonist 5'-(N-ethyl-carboxamido)-adenosine (NECA) had no effect. ATPgammaS was about equieffective with **ATP**, whereas alpha,beta-methylene-**ATP** (**APCPP**) did not induce sup 4sup 5Casup 2sup + influx. **Stimulation** of sup 4sup 5Casup 2sup + influx by **ATP** was not abolished by the dihydropyridine Casup 2sup + channel antagonist darodipine (PY 108-068), which completely blocked depolarization-induced sup 4sup 5Casup 2sup + influx. Inorganic cations (Lasup 3sup +, Cdsup 2sup +, Cosup 2sup +, Nisup 2sup +, Mnsup 2sup +, and Mgsup 2sup +) were able to inhibit both agonist- and depolarization-induced sup 4sup 5Casup 2sup + influx. Cdsup 2sup +, however, was ~20 times more selective in blocking Ksup +-stimulated than agonist-stimulated sup 4sup 5Casup 2sup + influx. These data indicate that ATP-stimulated Casup 2sup + influx in rat aortic smooth muscle cells is resistant to darodipine but is reduced by Lasup 3sup +, Cdsup 2sup +, and other inorganic blockers of Casup 2sup + channels.

6/7/30 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11567798 98703325 PMID: 11365019
Restoring antigen presentation: the first step on the road to complete immune restoration.
Konlee M
Positive health news (UNITED STATES) Spring 1998, (No 16) p7-12,
Journal Code: 9890538
Document type: Newspaper Article
Languages: ENGLISH
Main Citation Owner: NLM
Abstract Source: AIDS
Record type: Completed
Successful restoration of the immune system and eradication of any chronic infection, possibly including cancer, requires the ability of healthy cells to process and present foreign antigens on the cell's surface. Areas **addressed** include: (1) defining a foreign antigen; (2) discussing how certain viruses, such as HIV, can evade an effective immune response; and (3) describing factors that depress **antigen presentation**, i.e., low **ATP** and L-glutathione levels. Excerpts from a report on the use of glutathione and **ATP** injections for improving immune function in patients with Chronic Fatigue Immune Dysfunction Syndrome (CFID) are presented. Results indicate that 226 out of 276 patients receiving injections reported less fatigue, 196 experienced improvement in memory and concentration, and 171 experienced lower levels of pain. Comments from CFID patients who used injectable glutathione are included. The link between high viral load, loss of DTH, and low glutathione levels is discussed. Using selenium to increase glutathione levels, lower beta 2 microglobulin levels, fight cancer, and improve survival in AIDS is also discussed. The reasons that cell metabolism needs healthy liver function and coenzymated B vitamins are given. Products and protocols that can improve ATP production, cell metabolism, and increased levels of glutathione and the treatments and factors that improve, and suppress, antigen presentation are summarized.
Record Date Created: 19980505
Record Date Completed: 19980505

6/7/31 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11119048 97413363 PMID: 9269778
Presentation of exogenous protein antigens on major histocompatibility complex class I molecules by dendritic cells: pathway of presentation and regulation by cytokines.
Brossart P; Bevan M J
Howard Hughes Medical Institute, Department of Immunology, University of Washington, Seattle 98195, USA.
Blood (UNITED STATES) Aug 15 1997, 90 (4) p1594-9, ISSN 0006-4971 Journal Code: 7603509
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Several recent studies have shown that dendritic cells (DC) pulsed with soluble proteins can present peptide epitopes derived from these exogenous antigens on major histocompatability complex (MHC) class I molecules and induce an antigen-specific cytotoxic T lymphocyte (CTL) response. We provide evidence here that DC use macropinocytosis to capture soluble antigens that are then presented on MHC class I molecules. The presentation of an epitope derived from soluble ovalbumin was transporter associated with antigen presentation (TAP)-dependent, brefeldin A-sensitive, blocked by inhibitors of proteasomes, and resistant to chloroquine. These data suggest that exogenous antigens access the cytosol of DC and are proccessed for presentation via the same pathway described for conventional MHC class I-restricted cytosolic antigens. Proinflammatory mediators such as tumor necrosis factor-alpha (TNF-alpha) and lipopolysaccharide (LPS) reduced the efficiency of ovalbumin presentation via this pathway. This reduced presentation was not due to impaired expression of class I molecules because these substances upregulated the cell surface expression of Kb-molecules comparable to levels induced by interferon-gamma (IFN-gamma) treatment. The addition of IFN-gamma increased ovalbumin presentation even in the presence of TNF-alpha or LPS. These results show that DC might be involved in the cross-priming phenomenon. This could offer the immune system an additional pathway for effective priming of cytotoxic T cells and provide the possibility to activate both CD4 and CD8 T-cell responses.
Record Date Created: 19970924
Record Date Completed: 19970924

6/7/32 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10721314 97070728 PMID: 8913654
Requirements for HLA-B*2705-binding peptides with special regard to the transporter associated with antigen processing (TAP).
Kuipers J G; Raybourne R; Williams K M; Zeidler H; Yu D T
Abteilung Rheumatologie, Medizinische Hochschule, Hannover, Germany.
Clinical and experimental rheumatology (ITALY) Sep-Oct 1996, 14 (5) p523-9, ISSN 0392-856X Journal Code: 8308521
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
OBJECTIVE: To refine the algorithms governing peptide presentation by HLA-B*2705 by analyzing: (i) the specificity of the human transporter associated with antigen processing (TAP) for HLA-B27 binding peptides; and (ii) the peptide binding affinity to HLA-B*2705. METHODS: TAP-translocation

was measured with a labeled reporter peptide containing an N-linked glycosylation acceptor site in Streptolysin O-permeabilized cells for a panel of HLA-B27 binding peptides. Peptide binding affinity was determined by peptide-induced stabilization of empty HLA-B*2705 expressed by the TAP-deficient cell line T2-B27. RESULTS: Human TAP preferentially translocated analogues with residues leucine, isoleucine, methionine and arginine as the carboxy-terminal amino acids, whereas analogues with aspartic acid and serine were translocated poorly. The binding affinity to HLA-B*2705 of the poorly translocated aspartic acid and serine analogues was about 100-fold less compared to the parent HLA-B27 binding peptide. CONCLUSIONS: Human TAP shows considerable specificity for the C-terminus of potential HLA-B27 ligands. Nonamer peptides with aspartic acid and serine at the C-terminus are poorly translocated by the TAP and have low binding affinity for HLA-B*2705, and are therefore unlikely to become presented by HLA-B*2705.

Record Date Created: 19970220

Record Date Completed: 19970220

6/7/33 (Item 4 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10205482 96006575 PMID: 7590974

Polymorphic peptide transporters in MHC class I monomorphic Syrian hamster.

Lobigs M; Rothenfluh H S; Blanden R V; Mullbacher A

Division of Cell Biology, John Curtin School of Medical Research, Australian National University, P. O. Box 334, Canberra, ACT 2601, Australia.

Immunogenetics (UNITED STATES) 1995, 42 (5) p398-407, ISSN 0093-7711 Journal Code: 0420404

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

We have already shown that in species with highly polymorphic major histocompatibility complex (MHC) class I molecules (human, mouse) no functional polymorphism of the peptide transporters TAP1 and TAP2 is detectable (Lobigs and Mullbacher 1993). Investigating the antigen-presentation machinery of the class I MHC monomorphic Syrian hamster using mouse MHC class I expression via recombinant vaccinia viruses (VV) we found that six hamster cell lines fall into two phenotypic classes. four cell lines (HaK, FF, MF-2, and HT-1) showed no defect in expressing four different H2 class I molecules (Kk, Kd, Kb, Dd) and the appropriate VV peptide recognized by mouse VV-immune cytotoxic T (Tc) cells on the cell surface. Two cell lines (BHK-21 and NIL-2) expressed Dd and Kb in association with VV peptides as recognized by VV-immune, H2-restricted Tc cells but not Kk and Kd. However, Kd was expressed on the cell surface, as shown by fluorescence-activated cell sorter (FACS) analysis and alloreactive Tc-cell recognition. Kk is only surface-expressed in these two cell lines when superinfected with two VV recombinants encoding rat TAP1 (VV-mtp1) and TAP2 (VV-mtp2). Superinfection with VV-mtp1 and VV-mtp2 rendered both cell lines, after infection with either VV-Kk and VV-Kd, susceptible to lysis by either Kk- or Kd-restricted VV-immune Tc cells. Thus Syrian hamster cell lines express functionally polymorphic peptide transporters. The TAP2 gene from FF cells was cloned and sequenced; comparison with human, mouse, and rat TAP2 sequences show 78%, 88% and 87% similarity, respectively.

Record Date Created: 19951207

Record Date Completed: 19951207

6/7/34 (Item 5 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

10034240 21970272 PMID: 11972874
Calreticulin binds to the alpha1 domain of MHC class I independently of tapasin.
Turnquist H R; Vargas S E; McIlhaney M M; Li S; Wang P; Solheim J C
Eppley Institute for Research in Cancer and Allied Diseases, University of Nebraska Medical Center, Omaha, Nebraska 68198-6805, USA.
Tissue antigens (Denmark) Jan 2002, 59 (1) p18-24, ISSN 0001-2815 Journal Code: 0331072
Contract/Grant No.: GM57428; GM; NIGMS; T32 CA09476; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Prior to binding to antigenic peptide, the major histocompatibility complex (MHC) heavy chain associates with an assembly complex of proteins that includes calreticulin, tapasin, and the transporter associated with antigen processing (TAP). Our data show that calreticulin can bind weakly to Ld without tapasin's assistance, and that deglycosylation of the alpha1 domain results in a primary loss of binding to calreticulin rather than tapasin. We have also shown that high amounts of wild-type tapasin are still unable to associate with MHC class I in the absence of the MHC class I/calreticulin interaction, confirming the central role of calreticulin in the formation of the MHC class I assembly complex.
Record Date Created: 20020425
Record Date Completed: 20021016

6/7/35 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09352340 21113745 PMID: 11159003
IFN-beta mediates coordinate expression of antigen-processing genes in RSV-infected pulmonary epithelial cells.
Jamaluddin M; Wang S; Garofalo R P; Elliott T; Casola A; Baron S; Brasier A R
Department of Medicine, The University of Texas Medical Branch, Galveston, Texas 77555-1060, USA.
American journal of physiology. Lung cellular and molecular physiology (United States) Feb 2001, 280 (2) pL248-57, ISSN 1040-0605 Journal Code: 100901229
Contract/Grant No.: P30-ES-06676; ES; NIEHS; R01-AI-15939; AI; NIAID; R01-AI-40218; AI; NIAID; R30-HD-27841; HD; NICHD
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Major histocompatibility complex (MHC) class I-restricted cytotoxic T lymphocytes (CTLs) clear respiratory tract infections caused by the pneumovirus respiratory syncytial virus (RSV) and also mediate vaccine-induced pulmonary injury. Herein we examined the mechanism for RSV-induced MHC class I presentation. Like infectious viruses, conditioned medium from RSV-infected cells (RSV-CM) induces naive cells to coordinately express a gene cluster encoding the transporter associated with antigen presentation 1 (TAP1) and low molecular mass protein (LMP) 2 and LMP7. Neutralization of RSV-CM with antibodies to interferon (IFN)-beta largely blocked TAP1/LMP2/LMP7 expression, whereas anti-interleukin-1 antibodies were without effect, and recombinant IFN-beta increased TAP1/LMP2/LMP7 expression to levels produced by RSV-CM. LMP2, LMP7, and TAP1 expression were required for MHC class I upregulation because the irreversible proteasome inhibitor lactacystin or transfection with a competitive TAP1

inhibitor blocked inducible class I expression. We conclude that RSV infection coordinately increases MHC class I expression and proteasome activity through the paracrine action of IFN-beta to induce expression of the TAP1/LMP2/LMP7 locus, an event that may be important in the initiation of CTL-mediated lung injury.
Record Date Created: 20010222
Record Date Completed: 20010308

6/7/36 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08936764 20225665 PMID: 10760797
Innate and adaptive immunity to tumors: IL-12 is required for optimal responses.
Grufman P; Karre K
Microbiology and Tumor Biology Center, Karolinska Institutet, Stockholm, Sweden. Per.Grufman@mtc.ki.se
European journal of immunology (GERMANY) Apr 2000, 30 (4) p1088-93, ISSN 0014-2980 Journal Code: 1273201
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We have investigated the importance of endogenously produced IL-12 in innate and adaptive immunity to tumor transplants. The immunogenic lymphoma RMA and its TAP-deficient variant RMA-S were tested for rejection responses by normal and IL-12-deficient mice. IL-12 was crucial for the immunity induced by one immunization with irradiated RMA cells, as well as for in vivo priming of a CTL response in mixed lymphocyte tumor cultures against this MHC class I-expressing tumor. The defective in vivo response could be overcome by multiple immunizations. In further studies of in vitro CTL responses, we found that IL-12 production from either the antigen-pulsed dendritic cells or from host cells was necessary to obtain strong CTL responses. In the complete absence of IL-12, no or only very weak responses could be detected. NK cell-mediated innate resistance, as assessed in non-immunized mice inoculated with a threshold dose of RMA-S cells, also required IL-12. However, NK cells with reduced activity were present in IL-12-deficient mice and contributed to innate resistance, as demonstrated with lower cell dose challenges. In conclusion, IL-12 is required for optimal adaptive and innate responses against tumors.
Record Date Created: 20000525
Record Date Completed: 20000525

6/7/37 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08908679 20196220 PMID: 10447725
Interleukin-3 and granulocyte-macrophage colony-stimulating factor enhance the generation and function of dendritic cells.
Storozynsky E; Woodward J G; Frelinger J G; Lord E M
Department of Microbiology and Immunology and Cancer Center Immunology Program, University of Rochester School of Medicine and Dentistry, Rochester, USA.
Immunology (ENGLAND) May 1999, 97 (1) p138-49, ISSN 0019-2805 Journal Code: 0374672
Contract/Grant No.: CA28332; CA; NCI; CA70218; CA; NCI; EY09638; EY; NEI; +
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM

Record type: Completed

Dendritic cells, well-known for their potent antigen-presenting activity, are generally present at very low frequency in the spleens of naive mice. We examined the ability of mice to generate functional dendritic cells (DC) following exposure to the cytokines interleukin-3 (IL-3) and granulocyte-macrophage colony-stimulating factor (GM-CSF). Tumours secreting these cytokines provided a continuous stimulus resulting in a greatly increased number and frequency of DC in the spleen. These cells were purified by conventional DC isolation techniques and were found to exhibit many of the characteristics of DC from unmanipulated mice, including high allo-stimulatory activity in mixed lymphocyte reactions and expression of many similar cell surface markers. Using ovalbumin-peptide specific class I- and class II-restricted hybridomas containing the lacZ reporter gene, we found that these cytokine-generated DC had a greatly increased efficacy in the uptake and processing of particulate antigen. These cells appear to have retained the ability to ingest antigen that is generally associated with immature DC, but also exhibit the peptide/major histocompatibility complex (MHC)-presenting capabilities of mature DC. Development of an assay to measure the activity of a single DC revealed that these dual activities were the properties of the majority of the cytokine-generated DC. These findings indicate that exposure in vivo to the cytokines IL-3 and GM-CSF can result in the generation of large numbers of DC with increased capability of stimulating T cells. Thus, these cells may be important in vivo in the process of cross-priming and the subsequent generation of tumour-reactive cytotoxic T lymphocytes (CTL).

Record Date Created: 20000404

Record Date Completed: 20000404

6/7/38 (Item 9 from file: 155)

DIALOG(R)File 155:MEDLINE(R)

08687853 95376458 PMID: 7544229

Up-regulation of MHC class I by flavivirus-induced peptide translocation into the endoplasmic reticulum.

Mullbacher A; Lobigs M

Division of Cell Biology, John Curtin School of Medical Research, Australian National University, Canberra.

Immunity (UNITED STATES) Aug 1995, 3 (2) p207-14, ISSN 1074-7613 Journal Code: 9432918

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: Completed

Flavivirus infection of mammalian cells increases the cell surface expression of major histocompatibility complex (MHC) class I molecules, the recognition elements for cytotoxic T cells. Here, we show that the mechanism for flavivirus-induced up-regulation of class I MHC involves an increase in peptide supply to the endoplasmic reticulum. Flavivirus-mediated peptide supply for MHC class I assembly is independent of the peptide transporters for class I antigen presentation, since infection of class I MHC peptide transport-deficient cell lines with flaviviruses results in the cell surface expression of biologically functional class I MHC peptide complexes. The flavivirus-induced supply of antigenic peptides to the endoplasmic reticulum is not restricted to flavivirus-encoded peptides and independent of interferon. The data imply that peptide availability regulates surface expression of class I MHC restriction elements and suggests a mechanism for flavivirus-induced immunopathology.

Record Date Created: 19950928

Record Date Completed: 19950928

6/7/39 (Item 10 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08449594 95137783 PMID: 7530699
CD1 expression is not affected by human peptide transporter deficiency.
Hanau D; Fricker D; Bieber T; Esposito-Farese M E; Bausinger H; Cazenave J P; Donato L; Tongio M M; de la Salle H
Histocompatibility Laboratory, Regional Center for Blood Transfusion, Strasbourg, France.
Human immunology (UNITED STATES) Sep 1994, 41 (1) p61-8, ISSN 0198-8859 Journal Code: 8010936
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Conventional major histocompatibility complex class I molecules are highly polymorphic and present peptides to cytotoxic T cells. These peptides derive from the proteolytic degradation of endogenous proteins in the cytosol and are translocated into the endoplasmic reticulum by a peptide transporter consisting of two transporter associated with antigen processing (TAP) molecules. Absence of this transporter leads to the synthesis of unstable peptide free class I molecules that are weakly expressed on the cell surface. Mouse nonconventional class I molecules (class Ib) may also present TAP-dependent peptides. In humans, CD1 antigens are nonconventional class I molecules. Recently, we characterized a human HLA class I deficiency resulting from a homozygous TAP deficiency. We show here that CD1a and -c are normally expressed on epidermal Langerhans cells of the TAP-deficient patients, as are CD1a, -b, and -c on dendritic cells differentiated in vitro from monocytes. Moreover, the CD1a antigens present on the surface of the dendritic cells are functional, since they internalize by receptor-mediated endocytosis gold-labeled F(ab')2 fragments of an anti-CD1a mAb. This suggests either that CD1 molecules are empty molecules, that they are more stable than empty conventional class I proteins, or that CD1 molecules present TAP-independent peptides.
Record Date Created: 19950302
Record Date Completed: 19950302

6/7/40 (Item 11 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07487711 92351278 PMID: 1641758
Energetics of defective macrophage antigen presentation after hemorrhage as determined by ultraresolution 31P nuclear magnetic resonance spectrometry: restoration with adenosine triphosphate-MgCl2.
Meldrum D R; Ayala A; Chaudry I H
Department of Surgery, Michigan State University, East Lansing 48824-1315.
Surgery (UNITED STATES) Aug 1992, 112 (2) p150-6; discussion 156-8, ISSN 0039-6060 Journal Code: 0417347
Contract/Grant No.: R01 GM37127; GM; NIGMS
Erratum in Surgery 1992 Oct;112(4) 846
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
BACKGROUND. The purpose of this study was to determine whether a decrease in macrophage energetics contributes to the profound immune dysfunction that occurs after hemorrhage and, if so, whether adenosine triphosphate (ATP)-MgCl2 treatment has any beneficial effects on the above parameters. METHODS. C3H/HeN mice were bled to a mean blood pressure of 35 mm Hg, maintained at that pressure for 60 minutes, resuscitated with their own

shed blood and Ringer's lactate, and treated with ATP-MgCl2 (80 mumol/kg body weight) or saline solution (vehicle). Peritoneal macrophages were harvested 1 hour after resuscitation and **ATP** levels were determined by 31P nuclear magnetic resonance spectrometry. In **addition**, macrophage functions were determined by measuring **antigen presentation** capacity (AP), as well as interleukin-1 (IL-1), interleukin-6 (IL-6), and tumor necrosis factor (TNF) synthesis. RESULTS. Hemorrhage caused a significant decrease in peritoneal macrophage AP function, as well as IL-1, IL-6, and TNF synthesis, by 52% +/- 14%, 91% +/- 12%, 78% +/- 8%, and 89% +/- 8%, respectively, which was correlated with a 78% +/- 6% decrease in macrophage ATP levels (p less than 0.05). Treatment with ATP-MgCl2 after hemorrhage restored macrophage ATP levels (p less than 0.05) and significantly increased (p less than 0.05) macrophage AP, IL-1, IL-6, and TNF release by 110% +/- 21%, 130% +/- 38%, 124% +/- 17%, and 66% +/- 24%, respectively. CONCLUSIONS. The decreased macrophage ATP levels may be the cause of defective macrophage AP and cytokine release after hemorrhage, and both macrophage ATP levels and macrophage immune functions can be restored with adjuvant ATP-MgCl2 treatment after hemorrhage.
Record Date Created: 19920828
Record Date Completed: 19920828

6/7/41 (Item 12 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06399380 90023815 PMID: 2679123
Differential blockade of agonist- and depolarization-induced 45Ca2+ influx in smooth muscle cells.
Wallnofer A; Cauvin C; Lategan T W; Ruegg U T
Preclinical Research, Sandoz Limited, Basel, Switzerland.
American journal of physiology (UNITED STATES) Oct 1989, 257 (4 Pt 1) pC607-11, ISSN 0002-9513 Journal Code: 0370511
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
ATP stimulated 45Ca2+ influx in rat aortic smooth muscle cells in a concentration-dependent manner (EC50 = 3.6 +/- 0.5 X 10(-7) M). ADP and GTP were less effective than ATP in **stimulating** 45Ca2+ influx; AMP was weakly active and the adenosine agonist 5'-(N-ethyl-carboxamido)-adenosine (NECA) had no effect. **ATP** gamma S was about equieffective with **ATP**, whereas alpha,beta-methylene-**ATP** (**APCPP**) did not induce 45Ca2+ influx. **Stimulation** of 45Ca2+ influx by **ATP** was not abolished by the dihydropyridine Ca2+ channel antagonist darodipine (PY 108-068), which completely blocked depolarization-induced 45Ca2+ influx. Inorganic cations (La3+, Cd2+, Co2+, Ni2+, Mn2+, and Mg2+) were able to inhibit both agonist- and depolarization-induced 45Ca2+ influx. Cd2+, however, was approximately 20 times more selective in blocking K+-stimulated than agonist-stimulated 45Ca2+ influx. These data indicate that ATP-stimulated Ca2+ influx in rat aortic smooth muscle cells is resistant to darodipine but is reduced by La3+, Cd2+, and other inorganic blockers of Ca2+ channels.
Record Date Created: 19891121
Record Date Completed: 19891121

6/7/42 (Item 13 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

03554601 81246848 PMID: 7019855
The properties of ATP-analogs in initiation of RNA synthesis catalyzed by RNA polymerase from E coli.

Smagowicz W J; Scheit K H
Nucleic acids research (ENGLAND) May 25 1981, 9 (10) p2397-401,
ISSN 0305-1048 Journal Code: 0411011
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Various base and sugar modified derivatives of **ATP** and UTP were used as substrate analogs for the steady state initiation reaction **ATP**+UTP=pppApU and the single step **addition** reaction **ApC**+ **ATP**=**ApCpA** . These reactions were carried out by E. coli RNA polymerase on T7 DNA in the presence of rifampicin. The steady state kinetic parameters of the analogs, either as substrates or inhibitors, were determined. On the basis of the obtained results it is concluded that purine NTP s in initiation require anti-conformation about the glycosidic bonds as well as gauche-gauche conformation of the C(4')-C(5') bonds. The latter conformation is also a prerequisite for substrates in elongation, whereas strict anti-conformation of glycosidic bonds is not.
Record Date Created: 19810915
Record Date Completed: 19810915

6/7/43 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

134265111 CA: 134(19)265111d JOURNAL
Extracellular ATP induces a distorted maturation of dendritic cells and inhibits their capacity to initiate Th1 responses
AUTHOR(S): La Sala, Andrea; Ferrari, Davide; Corinti, Silvia; Cavani, Andrea; Di Virgilio, Francesco; Girolomoni, Giampiero
LOCATION: Laboratory of Immunology, Instituto Dermopatico dell'Immacolata, Istituto di Ricovero e Cura a Carattere Scientifico, 00167 , Rome, Italy
JOURNAL: J. Immunol. DATE: 2001 VOLUME: 166 NUMBER: 3 PAGES: 1611-1617 CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists
SECTION:
CA215010 Immunochemistry
IDENTIFIERS: ATP dendritic cell maturation Th1 cell stimulation
DESCRIPTORS:
Lipopolysaccharides...
bacterial; extracellular ATP enhances dendritic cell expression of maturation markers induced by
Glycoproteins,specific or class...
CD40-L (antigen CD40 ligand), sol.; extracellular ATP enhances dendritic cell expression of maturation markers induced by
CD antigens...
CD83; extracellular ATP enhanced dendritic cell expression of
Dendritic cell...
effect of extracellular ATP on maturation and antigen presenting function of
Antigen presentation...
effect of extracellular ATP on maturation and antigen presenting function of dendritic cells
CD80(antigen)... CD86(antigen)...
extracellular ATP enhanced dendritic cell expression of
Interleukin 1.alpha.... Interleukin 1.beta.... Interleukin 12...
Interleukin 6... Tumor necrosis factors...
extracellular ATP inhibits dendritic cell prodn. of
Interferons...
.gamma.; decreased prodn. by T-cells on allostimulation by ATP-treated dendritic cells
T cell(lymphocyte)...

helper cell/inducer, TH1; extracellular ATP inhibits allostimulatory activity of dendritic cells for
Cell adhesion molecules...
ICAM-1 (intercellular adhesion mol. 1); extracellular ATP enhanced dendritic cell expression of
Cytokines...
inflammatory; extracellular ATP inhibits dendritic cell prodn. of
Interleukin 10... Interleukin 4... Interleukin 5...
prodn. by T-cells on allostimulation by ATP-treated dendritic cells
Purinoceptors...
P2X; in effect of extracellular ATP on maturation and antigen presenting function of dendritic cells
CAS REGISTRY NUMBERS:
56-65-5 biological studies, effect of extracellular ATP on maturation and antigen presenting function of dendritic cells

6/7/44 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

134040891 CA: 134(4)40891h JOURNAL
Extracellular ATP and TNF-.alpha. synergize in the activation and maturation of human dendritic cells
AUTHOR(S): Schnurr, Max; Then, Florian; Galambos, Peter; Scholz, Christoph; Siegmund, Britta; Endres, Stefan; Eigler, Andreas
LOCATION: Division of Clinical Pharmacology, Department of Medicine, Ludwig-Maximilians-University of Munich, Munich, Germany,
JOURNAL: J. Immunol. DATE: 2000 VOLUME: 165 NUMBER: 8 PAGES: 4704-4709 CODEN: JOIMA3 ISSN: 0022-1767 LANGUAGE: English PUBLISHER: American Association of Immunologists
SECTION:
CA215005 Immunochemistry
IDENTIFIERS: dendritic cell activation ATP TNF
DESCRIPTORS:
T cell(lymphocyte)...
activation; role of extracellular ATP and TNF-.alpha. in endocytosis, activation, IL-12 secretion, and T cell stimulatory capacity of dendritic cells
Cell adhesion molecules...
ICAM-1 (intercellular adhesion mol. 1); role of extracellular ATP and TNF-.alpha. in endocytosis, activation, IL-12 secretion, and T cell stimulatory capacity of dendritic cells
Histocompatibility antigens...
MHC (major histocompatibility complex), class II; role of extracellular ATP and TNF-.alpha. in endocytosis, activation, IL-12 secretion, and T cell stimulatory capacity of dendritic cells
Purinoceptors...
P2; role of extracellular ATP and TNF-.alpha. in endocytosis, activation, IL-12 secretion, and T cell stimulatory capacity of dendritic cells
CD86(antigen)... Dendritic cell... Endocytosis... Interleukin 12... Tumor necrosis factors...
role of extracellular ATP and TNF-.alpha. in endocytosis, activation, IL-12 secretion, and T cell stimulatory capacity of dendritic cells
CAS REGISTRY NUMBERS:
56-65-5 biological studies, role of extracellular ATP and TNF-.alpha. in endocytosis, activation, IL-12 secretion, and T cell stimulatory capacity of dendritic cells
? ds

Set	Items	Description
S1	192	(DENDRITIC)(20N)(THERAP? OR TREAT?)(30N)(CORRELAT? OR PREDICT?)

```
S2          96   RD S1 (unique items)
S3           0   S2 AND ATP
S4         459   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
S5          81   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)(10N)(A-
                 DD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
S6          44   RD S5 (unique items)
? s s2 and (disease? or immunity or viral or bacterial or cancer?)
Processing
```

ds

```
Set     Items   Description
S1        192   (DENDRITIC)(20N)(THERAP? OR TREAT?)(30N)(CORRELAT? OR PRED-
                ICT?)
S2         96   RD S1 (unique items)
S3          0   S2 AND ATP
S4        459   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
S5         81   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)(10N)(A-
                DD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
S6         44   RD S5 (unique items)
? s s2 and (disease? or immunity or viral or bacterial or cancer?)
Processing
             96  S2
        7276067  DISEASE?
         296156  IMMUNITY
         675542  VIRAL
         994285  BACTERIAL
        2005269  CANCER?
      S7      54  S2 AND (DISEASE? OR IMMUNITY OR VIRAL OR BACTERIAL OR
                  CANCER?)
? t s7/7/all

 7/7/1      (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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14274204 BIOSIS NO.: 200300268233

PRENATAL FACTORS CAN INFLUENCE FUNCTIONAL RECOVERY FROM NEONATAL CORTICAL INJURY IN RATS.

AUTHOR: Kolb B E(a); Gibb R L(a); Halliwell C(a); Hastings E(a); Waite W(a)
AUTHOR ADDRESS: (a)Canadian Centre for Behavioural Neuroscience, Univ Lethbridge, Lethbridge, AB, Canada**Canada

JOURNAL: Society for Neuroscience Abstract Viewer and Itinerary Planner 2002pAbstract No 3216 2002
MEDIUM: cd-rom
CONFERENCE/MEETING: 32nd Annual Meeting of the Society for Neuroscience Orlando, Florida, USA November 02-07, 2002
SPONSOR: Society for Neuroscience
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Rats given perinatal cortical lesions on postnatal days 1-5 show chronic deficits in cognitive and motor behavior. The behavioral deficits are **correlated** with small brain size, thin remaining neocortical mantle, and atrophy of **dendritic** arborizations in cortical pyramidal cells. Both the behavioral deficits and antomical abnormalities are attenuated by various postinjury **treatments** including tactile stimulation, complex housing, nicotine, bFGF, and a choline-enriched diet. Here we examine the behavioral and anatomical sequelae of day 3 (P3) frontal or parietal lesions in animals given the same treatments, as well as fluoxitine, presented prenatally rather than postnatally. Thus, animals were given the treatments prior to P3 lesions, and with the exception of choline treatment, all treatments ceased at birth. Prenatal treatments with nicotine, tactile stimulation, complex housing, and choline all reduced the effect of subsequent cortical injury. In contrast, fluoxitine produced a significantly worse outcome. (The behavioral effect of bFGF treatment is still under study.) All treatments except fluoxitine produced chronic increases in AChE in the cortex and increased overall brain weight. Fluoxitine decreased brain weight in both normal and injured brains. These results show that prenatal experience can affect brain development postnatally and, more importantly, can influence recovery of function after perinatal brain injury. These results suggest that infants at risk for perinatal injury (such as

premature birth or difficult birth) may benefit from a wide range of prenatal treatments but not fluoxitine.

7/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

14244129 BIOSIS NO.: 200300238158
Urine **dendritic** cells may **predict** recurrent bladder **cancer** in patients **treated** with intravesical BCG.
AUTHOR: Beatty John D(a); Jones Angela(a); English Nicholas R(a); North Margaret(a); Ogden Christopher W(a); Knight Stella C(a)
AUTHOR ADDRESS: (a)Antigen Presentation Research Group, Faculty of Medicine Imperial College London, Watford Rd, Northwick Park Campus, Harrow, HA1 3UJ, UK**UK
JOURNAL: Clinical Science (London) 104 (Supplement 49):p34P 2003
MEDIUM: print
CONFERENCE/MEETING: Spring Meeting of the Medical Research Society London, UK February 05, 2003
SPONSOR: Medical Research Society
ISSN: 0143-5221
RECORD TYPE: Citation
LANGUAGE: English

7/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

14238029 BIOSIS NO.: 200300232058
Dendritic cell monitoring during BCG immunotherapy: Can we **predict treatment** failures?
AUTHOR: Beatty John D(a); Smith Richard D(a); Knight Stella C(a); Ogden Christopher W(a)
AUTHOR ADDRESS: (a)Middlesex, UK**UK
JOURNAL: Journal of Urology 169 (4 Supplement):p130 April 2003 2003
MEDIUM: print
CONFERENCE/MEETING: 98th Annual Meeting of the American Urological Association (AUA) Chicago, IL, USA April 26-May 01, 2003
SPONSOR: American Urological Association
ISSN: 0022-5347
RECORD TYPE: Citation
LANGUAGE: English

7/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

14120306 BIOSIS NO.: 200300114335
Clinical effects of tumor-associated macrophages and dendritic cells on renal cell carcinoma.
AUTHOR: Hamada Ikuto(a); Kato Mikio; Yamasaki Tetsuo; Iwabuchi Kazuaki; Watanabe Toru; Yamada Takumi; Itoyama Shinji; Ito Hiroki; Okada Koichi
AUTHOR ADDRESS: (a)Department of Urology, Saitama Medical School, 38 Moro-Hongo, Moroyama, Irumagun, Saitama, 350-0451, Japan**Japan
JOURNAL: Anticancer Research 22 (6C):p4281-4284 November-December 2002 2002
MEDIUM: print
ISSN: 0250-7005
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Several reports have documented infiltration of many monocytes in renal cell carcinoma (RCC). Since few studies have examined the relationship between monocyte infiltration and clinical prognosis in RCC, we clinically investigated this relationship by semi-quantitative analysis of monocyte infiltration and tumor angiogenesis. The following six parameters were measured immunohistologically in 98 RCC patients who underwent nephrectomy between 1987 and 1997: tumor-associated macrophage (TAM), microvessel density (MVD), S-100 protein-positive cells (S-100(+) cells), HLA-DR-positive cells, apoptosis index and proliferative index (PI). We then assessed intercorrelations among parameters and correlations to prognosis. Significant positive correlations were identified for TAM, MVD and PI, with a tendency for higher parameter values to reflect poorer prognosis. The prognosis of patients without metastasis was poor for the high TAM group even when levels of MVD were low. These findings suggest that TAM facilitates the growth of RCC via angiogenesis and other mechanisms. Prognosis was significantly better in metastatic RCC patients who underwent interferon-alpha (IFN-alpha) **therapy** when the levels of S-100(+) cells were high. Nonetheless, the levels of S-100(+) cells among these IFN-**treated** patients did not **correlate** with other parameters, and none of the other parameters **correlated** with prognosis. One of the antitumor effects of IFN-alpha for RCC could therefore be mediated by **dendritic** cells.

7/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

14006393 BIOSIS NO.: 200300000422
Tumor suppression induced by intratumor administration of adenovirus vector expressing NK4, a 4-kringle antagonist of hepatocyte growth factor, and naive dendritic cells.
AUTHOR: Kikuchi Toshiaki(a); Maemondo Makoto; Narumi Koh; Matsumoto Kunio; Nakamura Toshikazu; Nukiwa Toshihiro
AUTHOR ADDRESS: (a)Department of Respiratory Oncology and Molecular Medicine, Institute of Development, Aging and Cancer, Tohoku University, 4-1 Seiryomachi, Aobaku, Sendai, 980-8575, Japan**Japan E-Mail: kikuchi@idac.tohoku.ac.jp
JOURNAL: Blood 100 (12):p3950-3959 December 1 2002 2002
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: NK4, a 4-kringle antagonist of hepatocyte growth factor (HGF), is a potent inhibitor of tumor angiogenesis and functions independently of its HGF-antagonistic activity. We have shown previously that in vivo genetic modification of tumors with an adenovirus vector that expresses NK4 (AdNK4) restrains tumor angiogenesis and slows the rate of tumor growth in vivo. In the present study, we investigated the hypothesis that this can be made more efficient by also administering bone marrow-generated **dendritic** cells (DCs) to the tumor. The data show that the growth of mouse subcutaneous tumors is significantly suppressed by direct administration of DCs into established tumors that had been pretreated with AdNK4 3 days previously. The synergistic antitumor effect produced by the combination **therapy** of AdNK4 with DCs **correlated** with the in vivo priming of tumor-specific cytotoxic T lymphocytes. Analysis of mice treated with fluorescence-labeled DCs suggested that DCs injected into the flank tumor could migrate to lymphoid organs in vivo for activation of immune-relevant processes. Knockout mice experiments demonstrated that the tumor regression produced

by this combination therapy depends on both major histocompatibility complex (MHC) class I antigen presentation of DCs injected into the tumors and CD8+ T cells of the treated host. Finally, a mechanism for this synergism was suggested by the histological observation that tumor necrosis and apoptosis were induced by genetic engineering of the tumors to express NK4. These findings should be useful in designing novel strategies that use a combination of 2 monotherapies directed against the vascular and immune systems for **cancer** therapy.

7/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13948577 BIOSIS NO.: 200200577398
Sezary syndrome patients demonstrate a defect in dendritic cell populations: Effects of CD40 ligand and treatment with GM-CSF on dendritic cell numbers and the production of cytokines.
AUTHOR: Wysocka Maria; Zaki Mohamed H; French Lars E; Chehimi Jihed; Shapiro Michael; Everetts Suzanne E; McGinnis Karen S; Montaner Luis; Rook Alain H(a)
AUTHOR ADDRESS: (a)Department of Dermatology, University of Pennsylvania, 3600 Spruce St, Philadelphia, PA, 19104**USA E-Mail: arook@mail.med.upenn.edu
JOURNAL: Blood 100 (9):p3287-3294 November 1, 2002
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Sezary syndrome (SzS) is an advanced form of cutaneous T-cell lymphoma associated with involvement of the peripheral blood by malignant T cells. The **disease** is defined by impaired cell-mediated **immunity** and the production of interferon-gamma (IFN-gamma) and interleukin-2 (IL-2), possibly as a result of deficient IL-12 production. To understand the mechanism of this impairment, we examined the composition and function of **dendritic** cells and monocytes in the blood of SzS patients with different levels of peripheral blood tumor burden. Consistent with our previous observations, numbers of monocytes in SzS patients were comparable to numbers observed in healthy donors. In contrast, decreased IL-12 production **correlated** with a decrease in the numbers of CD11c+ **dendritic** cells, which was particularly profound among patients with medium (20%-50% circulating malignant T cells) and high (more than 50% circulating malignant T cells) tumor burden. Furthermore, CD123+ **dendritic** cells, major producers of IFN-alpha, were significantly diminished in SzS patients, regardless of the level of tumor burden. Granulocyte macrophage-colony-stimulating factor-**treated** patients experienced an increase in the number of dendritic cells but not in IFN-alpha or IL-12 production. However, in vitro stimulation of peripheral blood mononuclear cells from SzS patients with rCD40L and IFN-gamma significantly increased the production of IL-12. Thus, our results demonstrate a profound defect in circulating dendritic cells in SzS patients that may contribute to the pathogenesis of the cytokine disorders and to the depressed cellular **immunity**. Importantly, the ability of rCD40L to potently induce IL-12 production from monocytes and residual dendritic cells of SzS patients could potentially serve as an immune-restorative therapeutic agent.

7/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13740306 BIOSIS NO.: 200200369127
Indoleamine 2,3-dioxygenase modulates T cell alloresponses.
AUTHOR: Johnson Theodore S(a); Keskin Derin(a); Jhaver Kanchan(a); Marshall Brendan(a); Mellor Andrew(a)
AUTHOR ADDRESS: (a)Institute of Molecular Medicine and Genetics, Medical College of Georgia, 1120 15th Street, Augusta, GA, 30912**USA
JOURNAL: FASEB Journal 16 (4):pA716 March 20, 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Catabolism of L-tryptophan by cells expressing functional indoleamine 2,3-dioxygenase (IDO) is a natural T cell suppressive mechanism that protects murine fetuses from lethal attack by maternal **immunity** during pregnancy. In work reported here, constitutive expression of IDO by MC57G fibrosarcoma cells is **correlated** to suppression of murine T cell alloresponses in vitro and in vivo. We also found that **dendritic** cells from IDO -/- mice stimulate augmented T cell responses in vitro, relative to **dendritic** cells from wild type littermates. Antigen specific immune suppression mediated by **dendritic** cell subsets may be a homeostatic mechanism to protect peripheral tissues from self-reactive T cells. Furthermore, IDO related modulation of T cell alloresponses may be important in the medical **treatment** of transplant recipients, **cancer** patients, or HIV patients. Therefore, over-expression or pharmacological inhibition of IDO may prove to be a viable therapeutic option, not only in the treatment of such patients, but also in treating autoimmune **diseases**.

7/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13724986 BIOSIS NO.: 200200353807
Estrogen induces OPG secretion and inhibits DC-LAMP expression in human dendritic cells.
AUTHOR: Bengtsson Asa Kristina(a); Ryan Elizabeth J(a); Magaletti Dario M (a); Clark Edward A(a)
AUTHOR ADDRESS: (a)Microbiology, University of Washington, 1705 NE Pacific, Seattle, WA, 98195**USA
JOURNAL: FASEB Journal 16 (4):pA320 March 20, 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Osteoprotegerin (OPG) is a secreted glycoprotein that binds to RANK ligand (RANKL) and TRAIL. OPG plays an important role in the immune system by regulating T- and **dendritic** cell (DC) interactions. Women are at much greater risk of developing certain autoimmune **diseases**, and fluctuations in the levels of estrogen **correlate** with **disease** status. To investigate the effect of estrogen on DCs, we **treated** human immature monocyte derived DCs (MDDCs) for 24 h with estrogen. We did not detect any phenotypic differences in the immature MDDCs after estrogen treatment. However, after activating MDDCs with CD40L we found a decreased DC-LAMP expression in the estrogen-pretreated MDDCs. Since DC-LAMP is a reliable marker to identify mature DCs, these data suggest that estrogen inhibits DC maturation. We found a significant increase in OPG production by MDDCs after CD40L stimulation.

Interestingly, estrogen treatment also significantly upregulated the production of OPG in MDDCs. DCs express RANK and TRAIL receptors. By binding TRAIL and RANKL, OPG can modify DC function, survival and death. The lifespan of mature DCs must be tightly regulated in order to avoid excessive immune responses. Data will be presented assessing the effect of estrogen on DC survival. In summary, estrogen may effect the RANK/RANKL/OPG and TRAIL/TRAIL-R/OPG systems in DCs, and this may be a contributing factor that put women at risk for DC dysregulation.

7/7/9 (Item 9 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13715079 BIOSIS NO.: 200200343900
Genetic mapping of cytotoxicity of dendritic cells against tumor cells using C57BL/6 X DBA/2 (BXD) BXD recombinant inbred (RI) strains of mice.
AUTHOR: Yang Xinwen(a); Hsu Hui-Chen; Grizzle William E; Sun Shiher; Yang PingAr; Yiu Zhong-Yu; Mountz John D; Zhang Huang-Ge
AUTHOR ADDRESS: (a)Department of Medicine, University of Alabama at Birmingham, 19th St. S, LHRB473, Birmingham, AL, 35294**USA
JOURNAL: FASEB Journal 16 (4):pA665-A666 March 20, 2002
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Professional Research Scientists on Experimental Biology New Orleans, Louisiana, USA April 20-24, 2002
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We utilized genotype well-defined 15 strains of BXD RI strains mice to determine if genetic loci underlie the dendritic cell response to the breast tumor cell line TS/A. Dendritic cells were assayed for tumor antigen processing, tumor cytotoxicity, and IL-12 induction. T cells isolated from BXD strain 9 (BXD9) of mice previously immunized with breast tumor TS/A cells were stimulated in vitro with dendritic cells isolated from 15 strains of BXD RI mice fed with TS/A tumor antigens for 3 days. Proliferation determined by (3H)-thymidine incorperation indicated that the ability of **dendritic** cells to stimulate T-cell proliferation greatly depended on BXD RI strain that was used as a stimulator. Furthermore, the phagocytosis capability of **dendritic** cells to tumor cells and induction of IL-12 in vitro were **correlated** (P<0.01) with the T-cell proliferative response stimulated by **dendritic** cells. Quantitative genetic mapping identified two loci that were associated with the processing of tumor antigens by dendrtic cells and the cytotoxicity response to the tumor cells. These loci may therefore provide novel targets to enhance **dendritic** cell-based **therapeutic** strategies.

7/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13591339 BIOSIS NO.: 200200220160
RITUXIMAB (Rab) and GM-CSF, an effective **therapy** for relapsed/refractory patients (pts) with low-grade B-cell lymphoma (L): **Correlation** between response and **dendritic** cell (DC) subpopulation mobilized.
AUTHOR: Rossi Jean-Francois(a); Yang Lu Zhao; Quittet Philippe(a); Navarro Robert(a); Legouffe Eric(a); Fegueux Nathalie(a); Crespy Lisa(a); Rouille Valerie(a); Klein Bernard
AUTHOR ADDRESS: (a)Hematology-Oncology, University Hospital Lapeyronie, Montpellier**France
JOURNAL: Blood 98 (11 Part 1):p607a November 16, 2001

MEDIUM: print
CONFERENCE/MEETING: 43rd Annual Meeting of the American Society of Hematology, Part 1 Orlando, Florida, USA December 07-11, 2001
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Rab is an anti-CD20 monoclonal antibody active in the treatment of L, particularly follicular (FL). Molecular response (R) is principally observed when Rab is used at diagnosis in combination with chemotherapy. DC are professional antigen presenting cells with a central role in control of **immunity**. They derive from hemopoietic cells, and may differentiate from monocytes under the action of cytokines or other molecules, including GM-CSF. Different cytokines are implicated in the process of DC/T helper polarization to host antigen presentation. 39 pts were included in this study. There were 29 FL, 4 mantle cell L, 4 Waldenstrom's **diseases** and 2 lymphocytic L. 22 pts were in relapse, 15 in progressive **disease** or refractory relapse, and 2 had stable **disease** at the inclusion. 80% had advanced **disease** (Stage III or IV) with 1 pt having leukemic expression, and 20% localized **disease** but with bulky tumor and/or compression. The mean time from diagnosis to inclusion was 57 months, with a mean of 2 previous lines of therapy including 10 pts who previously had autologous transplantation. 11 pts had positivity of bcl-2 PCR in the bone marrow and/or in the peripheral blood at the inclusion. Treatment included GM-CSF (5mug/kg per day (D), D1 to D8 s.c.) with I.V. administration of Rab at D5 at 375 mg/m2 every 21 days for 4 courses. Presently, 35 pts are evaluable for R. 14 pts were in complete R (CR) all having FL (40%), including the pt with the leukemic expression of the **disease**. 7 pts were in partial R (overall response rate: 60%), and 7 had minor R or stable **disease**. 5 pts experienced progressive **disease**. 5/11 pts had molecular R with negativation of the bcl-2 signal. 7 pts had a second course of the treatment followed by 3 additional Rs (1 CR and 2 PR). Median follow up is 19 months with sustained response for 13 patients in CR at 10 months+. We analyzed different biological parameters including the DC subpopulations in the peripheral blood (DC1/DC2, based on Lin-, CD14- and CD11c/CD123) for 25 pts at Day 0, Day 5 and D0 of the following course. Between D0 and D4, we observed an increase of WBC, monocytes, eosinophils and neutrophils and a decrease of lymphocytes and CD19+ cells. There was an inverse correlation (p=0.035) between CR and increase of DC2 subpopulation. GM-CSF and monoclonal antibodies represent an active combination with possible polarization of the immune system in responding pts.

7/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13268368 BIOSIS NO.: 200100475517
Deregulation of the expression of the fractalkine/fractalkine receptor complex in HIV-1-infected patients.
AUTHOR: Foussat Arnaud; Bouchet-Delbos Laurence; Berrebi Dominique; Durand-Gasselin Ingrid; Coulomb-L'Hermine Aurore; Krzysiek Roman; Galanaud Pierre; Levy Yves; Emilie Dominique(a)
AUTHOR ADDRESS: (a)Institut Paris-Sud sur les Cytokines, 32 Rue des Carnets, 92140, Clamart: emilie@ipsc.u-psud.fr**France
JOURNAL: Blood 98 (6):p1678-1686 September 15, 2001
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Fractalkine is the only member of the CX3C chemokine family. Polymorphism of the fractalkine receptor gene may influence the prognosis of human immunodeficiency virus (HIV) infection, but the nature of the cells expressing fractalkine or its receptor in HIV-infected patients remains unknown. We show that, in contrast to HIV-uninfected individuals, a large number of cells expressed fractalkine in T-cell zones of lymph nodes from HIV-infected patients. CD83+ mature and CD123+ plasmacytoid dendritic cells as well as plasma cells are involved in this increased expression of fractalkine. Increased numbers of plasmacytoid dendritic cells and plasma cells were present in T-cell zones of HIV-infected patients. CD83+ dendritic cells were present in similar number in HIV-infected patients and controls, but an increased fraction of these cells produced fractalkine in HIV-infected patients. Many plasma cells in the gut-associated lymphoid tissue from HIV-infected patients also produced fractalkine, whereas few cells produced fractalkine in the gut of controls. The fraction of CD45RO+ and CD45RO- T helper (Th) cells expressing the fractalkine receptor CX3CR1 was higher in HIV-infected patients than in healthy individuals, and these cells were abnormally sensitive to fractalkine stimulation. This increased response **correlated** with HIV viremia, and it returned to normal levels in patients successfully **treated** with antiretroviral drugs. The increased expression of the fractalkine/fractalkine receptor complex associated with HIV infection may affect adhesion and migration of Th lymphocytes and their interaction with **dendritic** cells. Thus, it may influence the equilibrium between depletion and renewal of the Th lymphocyte compartment.

7/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13130953 BIOSIS NO.: 200100338102
The phenotype of ascitic fluid lymphocytes in patients with ovarian carcinoma and other primaries.
AUTHOR: Melichar B(a); Touskova M; Tosner J; Kopecky O
AUTHOR ADDRESS: (a)Department of Oncology and Radiotherapy, Charles University Medical School and Teaching Hospital, Hradec Kralove**Czech Republic
JOURNAL: Onkologie 24 (2):p156-160 April, 2001
MEDIUM: print
ISSN: 0378-584X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English; German

ABSTRACT: Background: Ascitic tumor-infiltrating lymphocytes (TIL) are a potential source of effectors for adoptive immunotherapy. Patients and Methods: The TIL phenotype was examined by two-color flow cytometry in malignancy-related ascites of 49 patients with different primaries. Interleukin-10 (IL-10) and neopterin were determined in ascitic fluid by enzyme-linked immunoassay. Results: Malignant melanoma patients and significantly higher CD3+, CD3+CD8+ and CD3+CD95+, and lower CD3+CD4+ lymphocyte numbers than patients with other primaries. Ovarian **cancer** patients had higher CD3+CD45RO+, CD8+CD28+, CD19+CD86+, CD19+ and CD19+CD86+ lymphocyte numbers, and lower NK cell numbers than patients with gastrointestinal and pancreatic primaries. Pretreated patients had significantly lower concentrations of IL-10, lower CD8+CD28+, CD3+CD45RA+, and higher CD3+CD80+ numbers than chemotherapy-naive patients. Patients with hepatic metastases had lower CD3+, CD3+CD4+ and CD3+CD45RO+, and higher CD3+CD25+ and NK cell numbers than patients without liver metastases. A substantial number of cells

exhibited **dendritic** cell phenotype. Significant **correlations** were observed between neopterin and IL-10 concentrations, and numbers of CD8+CD28+ and CD3+CD80+ lymphocytes. Conclusions: Some parameters of TIL phenotype differ depending on primary, previous **treatment**, or the presence of liver metastases. A negative **correlation** was observed between IL-10 and neopterin, and an opposing effect of local concentrations of IL-10 and neopterin on the numbers of CD8+CD28+ and CD3+CD80+ was noted.

7/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13089202 BIOSIS NO.: 200100296351
Cortical plasticity and the development of behavior after early frontal cortical injury.
AUTHOR: Kolb Bryan(a); Gibb Robbin; Gorny Grazyna
AUTHOR ADDRESS: (a)Department of Psychology and Neuroscience, University of Lethbridge, Lethbridge, AB, T1K 3M4: kolb@uleth.ca**Canada
JOURNAL: Developmental Neuropsychology 18 (3):p423-444 2000
MEDIUM: print
ISSN: 8756-5641
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: It has been known for over 100 years that frontal lobe injury in children is often associated with considerably more functional recovery than after similar injury in adulthood. Systematic study of frontal cortical injury in laboratory animals has shown that this recovery is tightly tied to developmental age: There is a brief window of time during cortical development during which the brain is able to compensate. Simply being young is not sufficient because injury prior to this critical period leads to miserable behavioral outcomes. For humans, the least favorable time for cortical injury is likely at the end of the gestational period, perhaps including the 1st month or so of life whereas the most favorable time is around 1 to 2 years of age. In addition to age, the extent of behavioral recovery is influenced by age at assessment, the nature of the behavioral assessment, sex, and lesion size. Anatomical studies have shown that functional recovery following early cortical injury is **correlated** with a reorganization of remaining cortical circuitry, including increased **dendritic** arborization and increased spine density. Recovery, and the compensatory anatomical changes, can also be potentiated by application of different **treatments** including behavioral **therapy**, trophic factors, and neuromodulators. Finally, there is preliminary evidence in laboratory animals to suggest that it may be possible to induce neural regeneration in the injured brain and that the regenerated brain functions to support functional recovery.

7/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13073358 BIOSIS NO.: 200100280507
The serum soluble HLA-DR antigens as a predictive marker of the response to interferon-alpha treatment in patients with chronic hepatitis C.
AUTHOR: Hosoi Katsumi(a); Hagihara Masao; Kagawa Tatehiro; Watanabe Norihito; Matsuzaki Shohei
AUTHOR ADDRESS: (a)Department of Internal Medicine, Tokai University School of Medicine, Bohseidai, Isehara, Kanagawa, 259-1193:

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JOURNAL: Tokai Journal of Experimental and Clinical Medicine 25 (3):p 117-124 October, 2000
MEDIUM: print
ISSN: 0385-0005
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The serum concentrations of soluble HLA-DR antigens (sDR) were monitored in 40 patients with chronic hepatitis C (CHC) who received interferon treatment. The expression of HLA-class II antigens in liver tissues was also studied by immunohistochemistry. The sDR levels in patients with chronic hepatitis C were significantly higher than those in healthy subjects (416 +- 236 (mean +- S.D.) ng/ml vs. 286 +- 163 ng/ml) (P<0.05). There was no correlation between the sDR levels and serum alanine aminotransferase levels, suggesting that sDR do not reflect the extent of liver necrosis. Although there was no difference in pretreatment sDR levels between interferon complete responders and non-responders, sDR significantly declined in complete responders, while they did not in non-responders. The hepatic expression of HLA-DR antigens was observed in **dendritic** cells, lymphocytes and Kupffer cells in portal area, while in Kupffer cells and endothelial cells in central acinus. These expression significantly decreased in complete responders. From these results, sDR, reflecting the hepatic expression of HLA-DR antigens, could be a **predictive** marker of response to interferon **treatment**.

7/7/15 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13051159 BIOSIS NO.: 200100258308
Depletion of the pre-dendritic interferon-producing cell by corticosteroid administration in humans: Implications for mechanisms of steroid immunosuppression and pathogenesis of opportunistic infections.
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AUTHOR ADDRESS: (a)Saint Vincents Hospital and Medical Ctr, NYC, 153 West 11th Street, NY, NY, 10011**USA
JOURNAL: FASEB Journal 15 (5):pA1010 March 8, 2001
MEDIUM: print
CONFERENCE/MEETING: Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001 Orlando, Florida, USA March 31-April 04, 2001
ISSN: 0892-6638
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Failure of a specialized subset of blood MNC to produce interferon-alpha(IFN-alpha) in response to HSV **correlates** strongly with the onset of opportunistic infections (OI) in AIDS, and occurs in other **diseases** having high risk of OL. This IFN-alpha production defines the lin-CD11c-CD4+CD123+ plasmacytoid **dendritic** cell precursor subset. Because steroid **therapy**, like AIDS, induces reactivation of Ol in certain clinical settings, we studied the effect of glucocorticoids on the function and number of these cells. In a cross-sectional study, IFN-alpha production by MNC from patients given chronic or transient therapy with steroids for various clinical indications was significantly depressed during steroid administration (2.077 + 0.707 log10 IU/mL) compared to that of control MNC (3.226 + 0.329 log10 IU/mL, p<0.0005). IFN-alpha generation recovered within days

of stopping steroids. Single doses of prednisone had little effect. The doses of steroids employed, generally sufficient to control symptoms, produced only modest deviations of T cell subsets or T cell proliferation, and the expected alterations of granulocyte and lymphocyte counts. Incubation of MNC with steroids in vitro did not affect their ability to generate IFN-alpha. Serial FACS studies in normal volunteers showed prompt disappearance and then reappearance of the cells from blood during and after steroid administration with no change in the per-cell IFN generation. These striking changes on cell production, migration or differentiation likely play a role in the clinical immunosuppressive effects of steroids and contribute to susceptibility to OI.

7/7/16 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12773975 BIOSIS NO.: 200000527598
In vitro induction of tumor-specific human lymphocyte antigen class I-restricted CD8+ cytotoxic T lymphocytes by ovarian tumor antigen-pulsed autologous dendritic cells from patients with advanced ovarian **cancer**.
AUTHOR: Santin Alessandro D(a); Hermonat Paul L; Ravaggi Antonella; Bellone Stefania; Pecorelli Sergio; Cannon Martin J; Parham Groesbeck P
AUTHOR ADDRESS: (a)Division of Gynecologic Oncology, UAMS Medical Center, University of Arkansas, 4301 W Markham, Little Rock, AR, 72205-7199**USA
JOURNAL: American Journal of Obstetrics and Gynecology 183 (3):p601-609 September, 2000
MEDIUM: print
ISSN: 0002-9378
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: OBJECTIVE: The purpose of this study was to evaluate the potential of dendritic cells pulsed with whole-tumor extracts derived from autologous ovarian **cancer** cells in eliciting a tumor-specific cytotoxic T-cell response in vitro from patients with advanced ovarian **cancer**. STUDY DESIGN: CD8+ T lymphocytes stimulated in vitro with autologous ovarian tumor lysate-pulsed dendritic cells were tested for their ability to induce a human leukocyte antigen class I-restricted cytotoxic T-lymphocyte response able to specifically kill autologous tumor cells in standard 6-hour chromium 51 cytotoxicity assays. In addition, to correlate cytotoxic activity by cytotoxic T-lymphocytes with a particular lymphoid subset, 2-color flow cytometric analysis of intracellular cytokine expression (interferon gamma and interleukin 4) at the single-cell level was performed. RESULTS: Cytotoxic T lymphocytes specific for autologous ovarian tumor cells were elicited from 3 patients with advanced ovarian **cancer**. Although cytotoxic T-lymphocyte populations expressed strong cytolytic activity against autologous tumor cells, they did not lyse concanavalin A-stimulated autologous lymphocytes or autologous Epstein-Barr virus-transformed lymphoblastoid cell lines and showed negligible cytotoxicity against the natural killer cell-sensitive cell line K-562. Cytotoxic effect against the autologous tumor cells was inhibited by an anti-human leukocyte antigen class I monoclonal antibody (W6/32). It is interesting that CD8+ cytotoxic T lymphocytes expressed variable levels of CD56, a marker that may be associated with high cytotoxic activity. Finally, most of the tumor-specific CD8+ T cells exhibited a TH1 cytokine bias, and a high percentage of interferon gamma expressors among cytotoxic T lymphocytes was **correlated** with higher cytotoxic activity. CONCLUSION: These data show that tumor lysate-pulsed **dendritic** cells can consistently induce in vitro specific CD8+ cytotoxic T lymphocytes able to kill

autologous tumor cells from patients with advanced stage ovarian **cancer**. This novel approach may have important implications for the **treatment** of residual or resistant **disease** with active or adoptive immunotherapy after standard surgical and cytotoxic treatment.

7/7/17 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12562526 BIOSIS NO.: 200000316028
Treatment-induced decline of human immunodeficiency virus-1 p24 and HIV-1 RNA in lymphoid tissue of patients with early human immunodeficiency virus-1 infection.
AUTHOR: Kuster Herbert; Opravil Milos; Ott Peter; Schlaepfer Erik; Fischer Marek; Gunthard Huldrych F; Luthy Ruedi; Weber Rainer; Cone Richard W
AUTHOR ADDRESS: (a)Division of Infectious Diseases, Department of Internal Medicine, University Hospital, CH-8091, Zurich**Switzerland
JOURNAL: American Journal of Pathology 156 (6):p1973-1986 June, 2000
MEDIUM: print
ISSN: 0002-9440
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: We report detailed quantitative analysis of human immunodeficiency virus-1 (HIV-1) p24 and HIV-1 RNA in tonsil biopsies from 13 patients with early, asymptomatic HIV infection before and during combination antiretroviral **therapy**. Using fluorescent microscopy in conjunction with reverse transcriptase-polymerase chain reaction of frozen tissue sections, we show that plasma and tissue **viral** loads decreased by approximately 3 logs during the 1-year **treatment** period, with good **correlation** between the HIV-1 p24 and HIV-1 RNA response in tissue. The decrease of tissue **viral** load was delayed compared to plasma **viral** load, possibly explained by the observation that the amount of follicular **dendritic** cell-associated virus **correlated** best with the area under the curve of plasma HIV-1 RNA throughout the last 12 weeks. Before and during **treatment**, the relative proportions of HIV-1 on follicular **dendritic** cells and within mononuclear cells remained constant, suggesting similar decay characteristics in these two lymphoid tissue compartments. However, **viral** p24 or RNA remained almost always detectable in tissue despite full suppression of HIV-1 RNA in plasma, and increased even after short-term rebounds in plasma **viral** load. Thus, full and sustained suppression of **viral** replication was required to efficiently decrease **viral** load in lymphoid tissue, but complete abolition of residual **viral** replication was not achieved.

7/7/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12491717 BIOSIS NO.: 200000245219
Infiltrating dendritic/Langerhans cells in primary breast **cancer**.
AUTHOR: Tsuge Tohru; Yamakawa Mitsunori(a); Tsukamoto Masaru
AUTHOR ADDRESS: (a)First Department of Pathology, Yamagata University School of Medicine, 2-2-2 Iida-Nishi, Yamagata, 990-9585**Japan
JOURNAL: Breast Cancer Research and Treatment 59 (2):p141-152 Jan., 2000
ISSN: 0167-6806
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: It is fully anticipated that **dendritic** cells (DCs) will become a mainstay for inclusion in biological **therapies** for patients with **cancer** including breast **cancer**. To elucidate the cellular composition of DCs infiltrating human breast **cancers**, we investigated the **correlations** between the density of infiltrating DCs and some clinicopathological factors of breast **cancer** patients, examined cytokine expression on **cancer** cells and finally, assessed the numbers of CD45RO+ tumor infiltrating lymphocytes (TIL). Tissues adjacent to **cancer** nests contained significantly more S-100 protein+ and S-100 protein+ CD1a- DCs, but less CD1a+ DCs, than the nests. In invasive ductal carcinomas infiltration by S-100 protein+ DCs within and adjacent to nests, CD1a+ DCs within nests and S-100 protein+ CD1a- DCs adjacent to nests was denser than that in non-invasive carcinomas. With respect to the histological subtypes, there were fewer DCs in scirrhous carcinomas. Patients with stage IV **disease** had significantly fewer DCs of primary lesions than at other clinical stages. There were good correlations between infiltration by S-100 protein+ DCs and expression of the cytokines GM-CSF, IL-1alpha and TNF-alpha on **cancer** cells and between GM-CSF expression and S-100 protein+ CD1a- DCs. There was a close correlation between CD45RO+ TIL and S-100 protein+ DC densities both within and adjacent to the **cancer** nests and the S-100 protein+ CD1a- DC density adjacent to the **cancer** nests. Despite extensive immunoelectron microscopic observation, CD1a+ DCs within **cancer** nests contained only few Birbeck's granule-like structure. These data indicate that **cancer** nests are infiltrated predominantly by CD1a+ DCs, whereas S-100 protein+ CD1a- DCs predominate in surrounding tissues, and a infiltration by DCs may require cytokine expression on **cancer** cells and simultaneous lymphocyte infiltration. The findings of this clinicopathological study indicate the importance of evaluating simultaneously the types and localizations of infiltrating DCs in **cancer** tissues.

7/7/19 (Item 19 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12488727 BIOSIS NO.: 200000242229
In vitro evaluation of the sensitization potential of weak contact allergens using langerhans-like dendritic cells and autologous T cells.
AUTHOR: Rougier Nathalie; Redziniak Gerard; Mougin Danielle; Schmitt Daniel ; Vincent Claude(a)
AUTHOR ADDRESS: (a)Laboratoire de Recherche Peau Humaine et Immunite, INSERM Unite 346, Hopital Edouard Herriot, 69437, Lyon Cedex 03**France
JOURNAL: Toxicology 145 (1):p73-82 April 7, 2000
ISSN: 0300-483X
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Contact hypersensitivity is a major public health concern in most industrial countries, which is why **predictive** tests which could identify potential allergens are needed. We have established an in vitro approach for the detection of primary immune response. This model uses Langerhans-like **dendritic** cells (LLDC) derived from cord blood progenitors and autologous T lymphocytes, isolated from the same blood sample. **Treatment** of day 12-14 LLDC, with strong haptens trinitrobenzene sulfonic acid (TNP), fluorescein isothiocyanate (FITC) or Bandrowski's base (BB), results in the proliferation of T lymphocytes, whereas weak allergens and irritants, such as sodium dodecyl sulfate (SDS) are ineffective. The use of immature (day 8) LLDC and the addition

of a 48 h stage of incubation after hapten contact, result in phenotypic maturation of LLDC in addition to lymphocyte activation in all the cultures with strong haptens. The 48 h stage of incubation, results in sensitization and in some cases the induction of T cell proliferation to citronellal (1/8), coumarine (1/8) and to a prohapten p-phenylenediamine (pPDA; 2/8). The phenotype of DC after 48 h of contact with a strong hapten, becomes that of mature DC (CD83+, CD86+ and HLA-DR++). With fragrance molecules, weak haptens and prohaptens, a comparable phenotype is observed only when T lymphocytes are activated. These data suggest that the unresponsiveness observed with weak haptens, may be the consequence on an incomplete maturation of LLDC.

7/7/20 (Item 20 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12350589 BIOSIS NO.: 200000104091
Motoneuronal cell death is not correlated with aggregate formation of androgen receptors containing an elongated polyglutamine tract.
AUTHOR: Simeoni Silvia; Mancini Michael A; Stenoien David L; Marcelli Marco ; Weigel Nancy L; Zanisi Mariarosa; Martini Luciano; Poletti Angelo(a)
AUTHOR ADDRESS: (a)Istituto di Endocrinologia, Universita di Milano, Via Balzaretti 9, 20133, Milano**Italy
JOURNAL: Human Molecular Genetics 9 (1):p133-144 Jan., 2000
ISSN: 0964-6906
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Spinal and bulbar muscular atrophy (SBMA) is associated with an abnormal expansion of the (CAG)n repeat in the androgen receptor (AR) gene. Similar mutations have been reported in other proteins that cause neurodegenerative disorders. The CAG-coded elongated polyglutamine (polyGln) tracts induce the formation of neuronal intracellular aggregates. We have produced a model to study the effects of potentially 'neurotoxic' aggregates in SBMA using immortalized motoneuronal cells (NSC34) transfected with AR containing polyGln repeats of different sizes ((AR.Q(n = 0, 23 or 46)). Using chimeras of AR.Q(n) and the green fluorescent protein (GFP), we have shown that aggregate formation occurs when the polyGln tract is elongated and AR is activated by androgens. In NSC34 cells co-expressing the AR with the polyGln of pathological length (AR.Q46) and the GFP we have noted the presence of several dystrophic neurites. Cell viability analyses have shown a reduced growth/survival rate in NSC34 expressing the AR.Q46, whereas testosterone **treatment** partially counteracted both cell death and the formation of dystrophic neurites. These observations indicate the lack of **correlation** between aggregate formation and cell survival, and suggest that neuronal degeneration in SBMA might be secondary to axonal/**dendritic** insults.

7/7/21 (Item 21 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

12026246 BIOSIS NO.: 199900306765
In vivo and ex vivo gene therapy strategies to treat tumors using adenovirus gene transfer vectors.
AUTHOR: Crystal Ronald G(a)
AUTHOR ADDRESS: (a)520 East 70th Street, ST 505, New York, NY, 10021**USA
JOURNAL: Cancer Chemotherapy and Pharmacology 43 (SUPPL.):pS90-S99 May, 1999

ISSN: 0344-5704
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: The adaptation of gene therapy strategies to treat tumors has broadened the potential armamentarium of anticancer strategies to include approaches for local control of tumor growth as well as to enhance systemic antitumor **immunity** to treat metastases. A major focus of the author and colleagues has been to use replication-deficient adenovirus vectors, both in vivo and ex vivo, to enhance local control of and systemic **immunity** against **cancer**. Several examples will be used to demonstrate these strategies. Using prodrugs, systemically administered drugs converted to toxic metabolites in the local tumor milieu, has proven to be a useful strategy for achieving high local concentrations of the toxic product while avoiding the systemic toxicity that limits the use of chemotherapy agents. Transfer of genes encoding cytosine deaminase (with 5-fluorocytosine) and carboxylesterase (CE) (with irinotecan) are two paradigms that have been used in our laboratory. The data demonstrate that using adenoviruses to deliver these genes to the tumor site leads to production of the active chemotherapeutic agent, which diffuses from the cell in which it was produced to suppress tumor growth and attain regional control in a single organ. Extensive experimental and clinical data now exist to support the concept that tumor growth is critically dependent on angiogenesis and that vascular endothelial growth factor (VEGF) appears to play a central role in the process of tumor neovascularization. Data generated in our laboratory have shown that adenovirus-mediated regional anti-VEGF **therapy** using a gene encoding a soluble form of flt-1 (one of the VEGF receptors) can be used for regional control of tumor growth. The critical dependence of many tumors on VEGF for neovascularization and dissemination **predicts** the general applicability of this strategy for **treatment** of many solid tumors. Another paradigm involves **dendritic** cells, potent antigen-presenting cells that play a critical role in the initiation of antitumor immune responses. Immunization of mice with **dendritic** cells genetically modified using an adenovirus vector transferring a gene encoding a tumor antigen confers potent protection against a lethal tumor challenge, as well as suppression of preestablished tumors, resulting in a significant survival advantage. One clinical scenario to which this approach is relevant is treating micrometastases present at the time of primary detection of many malignancies. A possible clinical strategy would be to modify dendritic cells from such patients using an adenovirus vector encoding the relevant tumor antigen, and then administering the genetically modified dendritic cells as adjuvant treatment following primary therapy.

7/7/22 (Item 22 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11985657 BIOSIS NO.: 199900266176
Depletion in blood CD11c-positive dendritic cells from HIV-infected patients.
AUTHOR: Grassi Fernanda; Hosmalin Anne; McIlroy Dorian; Calvez Vincent; Debre Patrice; Autran Brigitte(a)
AUTHOR ADDRESS: (a)Laboratoire d'Immunologie Cellulaire et Tissulaire, URA CNRS 625, Hopital de la Pitie-Salpetrier**France
JOURNAL: AIDS (Hagerstown) 13 (7):p759-766 May 7, 1999
ISSN: 0269-9370
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: Objectives: To quantify blood dendritic cells from HIV-positive patients and to study the expression of functional molecules, in relation to HIV **viral** load, CD4 cell counts and antiretroviral treatment. Design and Methods: Three-colour flow cytometry analysis was used to quantify blood dendritic cells without previous isolation from whole blood and to study the expression of functional molecules (MHC class II, CD11c, CD83, CD86) by dendritic cells from 30 HIV-positive patients, 15 of whom were treated with combined antiretroviral therapy (**viral** loads from undetectable to 5.4 log copies/ml, CD4 cell counts 1-1895 cells/mm3) and 11 non-infected controls. Results: The median proportion of blood dendritic cells from HIV-positive patients was significantly decreased when the plasma **viral** load was above 200 copies/ml: 0.2% (0.1-1.1, n = 19) compared with 0.4% (0.2-0.8, n = 11) in patients with undetectable **viral** load whether they were treated or not, and to 0.4% (0.2-1.3, n = 11) in controls (P = 0.02). A major decrease of the CD11c positive dendritic cells was observed in all HIV-positive samples, with only 18% (mean; range: 0.3-80%, median 4.2%) compared with 44% (11-70%, median 42%) of control **dendritic** cells (P = 0.0006). In contrast, the proportion of **dendritic** cells expressing CD86, was slightly higher in HIV-positive patients than in controls (P = 0.03). Conclusions: The decreased proportion of blood **dendritic** cells **correlated** with virus replication and the lack of **dendritic** cells expressing CD11c are the first evidence of strong **dendritic** cell alterations in HIV-positive patients. Although the proportion of blood **dendritic** cells are in the normal range in **treated** HIV-positive patients with undetectable **viral** load, the CD11c alterations persist indicating that antiretroviral **therapy** might only partly correct the alterations of the circulating dendritic cells.

7/7/23 (Item 23 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11932835 BIOSIS NO.: 199900178944
Multi-antigen loaded **dendritic** cell (DC) vaccine for the **treatment** of metastatic renal cell carcinoma (mRCC) in-vitro **correlates**.
AUTHOR: Gitlitz Barbara; Hinkel Andreas; Mulders Peter; Tso Cho-Leo; Moldawer Nancy; Figlin Robert; Belledegrun Arie
AUTHOR ADDRESS: Los Angeles, CA**USA
JOURNAL: Journal of Urology 161 (4 SUPPL.):p137 April, 1999
CONFERENCE/MEETING: 94th Annual Meeting of the American Urological Association, Inc. Dallas, Texas, USA May 1-6, 1999
SPONSOR: American Urological Association
ISSN: 0022-5347
RECORD TYPE: Citation
LANGUAGE: English

7/7/24 (Item 24 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10931533 BIOSIS NO.: 199799552678
A pivotal role for glutamate in the pathogenesis of Schizophrenia, and its cognitive dysfunction.
AUTHOR: Hirsch Steven R(a); Das Indrajit; Garey Laurence J; De Belleroche Jacqueline
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JOURNAL: Pharmacology Biochemistry and Behavior 56 (4):p797-802 1997

ISSN: 0091-3057
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: There is mounting evidence of a glutamate dysfunction in schizophrenia, as suggested by the fact that schizophrenia and phencyclidine psychosis are similar and phencyclidine is known to block the N-methyl-D-aspartate (NMDA) subtypes of glutamate. Both occur mainly after puberty, suggesting they may share similar underlying developmental processes. Direct evidence is now accumulating from the study of messenger RNA that glutamate receptor deficiencies occur in schizophrenia and are regionally and specifically distributed. These results find support from studies of memory, electrophysiological findings, clinical **treatment**, and pharmacological studies in mammals and humans. Our recent findings of: a) a marked decrease in pyramidal cell **dendritic** spines in layer III of the frontal and temporal cortex, and b) a greater than 0.90 **correlation** between decrease in mRNA for the NMDA glutamate receptor and cognitive deterioration in elderly schizophrenics, present the strongest evidence to date that glutamate dysfunction plays an important role in schizophrenia.

7/7/25 (Item 25 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10899497 BIOSIS NO.: 199799520642
Antigen expression by **dendritic** cells **correlates** with the **therapeutic** effectiveness of a model recombinant poxvirus tumor vaccine.
AUTHOR: Bronte Vincenzo; Carroll Miles W; Goletz Theresa J; Wang Michael; Overwijk Willem W; Marincola Francesco; Rosenberg Steven A; Moss Bernard; Restifo Nicholas P(a)
AUTHOR ADDRESS: (a)Building 10, Room 2B42, Natl. Cancer Inst., 10 Center Drive, MSC 1502, Bethesda, MD 20892-1502**USA
JOURNAL: Proceedings of the National Academy of Sciences of the United States of America 94 (7):p3183-3188 1997
ISSN: 0027-8424
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recombinant poxviruses encoding tumor-associated antigens (TAA) are attractive as candidate **cancer** vaccines. Their effectiveness, however, will depend upon expression of the TAA in appropriate antigen-presenting cells. We have used a murine model in which the TAA is beta-galactosidase (beta-gal) and a panel of recombinant vaccinia viruses (rVV) in which beta-gal was expressed under early or late promoters at levels that varied over 500-fold during productive infections in tissue culture cells. Remarkably, only those rW employing early promoters were capable of prolonging the survival of mice bearing established tumors expressing the model TAA. Late promoters were ineffective regardless of their determined promoter strength. The best results were obtained when beta-gal was regulated by a strong early promoter coupled to a strong late promoter. When a variety of cell types were infected with the panel of viruses in vitro, dendritic cells were found to express beta-gal only under the control of the early promoters even though late promoters were intrinsically more active in other cell types. Furthermore, in a functional assay, dendritic cells infected in vitro with rVV encoding beta-gal regulated by an early promoter activated beta-gal-specific cytotoxic T lymphocytes, whereas similar rVV with a late promoter-regulated gene did not. These data indicate that promoter strength per se is not the most critical quality of a recombinant poxvirus-based tumor vaccine and that the use of promoters capable of

driving the production of TAA in "professional" antigen presenting cells may be crucial.

7/7/26 (Item 26 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10885103 BIOSIS NO.: 199799506248
Neurodegeneration and cognitive impairment in apoE-deficient mice is ameliorated by infusion of recombinant apoE.
AUTHOR: Masliah Eliezer(a); Samuel William; Veinbergs Isaac; Mallory Margaret; Mante Michael; Saitoh Tsunao
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JOURNAL: Brain Research 751 (2):p307-314 1997
ISSN: 0006-8993
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Recent studies suggest that apolipoprotein E (apoE) might play a neurotrophic function in the central nervous system and that altered functioning of this molecule could result in neurodegeneration. The main objective of this study was to determine if neurodegenerative and cognitive alterations in apoE-deficient mice are reversible by infusion of recombinant apoE into the lateral ventricles. ApoE-deficient mice **treated** with either apoE3 or apoE4 showed a significant improvement in their learning capacity in the Morris water maze compared to saline-infused apoE-deficient mice. While this improved performance was associated with restoration of neuronal structure, the poor learning ability of apoE-deficient mice **treated** with saline **correlated** with the disrupted synapto-**dendritic** structure. This study supports the contention that apoE might play a neurotrophic effect in vivo and suggests that apoE might have a potential **therapeutic** role.

7/7/27 (Item 27 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

08760249 BIOSIS NO.: 199395049600
HIV-1 LTR activation model: Evaluation of various agents in skin of transgenic mice.
AUTHOR: Morrey John D(a); Bourn Samuel M; Bunch Thomas D; Sidwell Robert W; Rosen Craig A
AUTHOR ADDRESS: (a)AIDS Res. Program, Dep. Animal Dairy and Veterinary Sci., Utah State Univ., Logan, Utah 84322-56**USA
JOURNAL: Journal of Acquired Immune Deficiency Syndromes 5 (12):p1195-1203 1992
ISSN: 0894-9255
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Mice containing the HIV-1 long terminal repeat (LTR) regulating the expression of firefly luciferase reporter gene were investigated for their use as a model for activation of the LTR. As a limited test of this model, a number of different factors were screened for their ability to affect reporter gene activities in the skin. Reporter gene levels were increased in the skin by topical treatment of dimethylsulfoxide, retinoic acid, phorbol ester, ultraviolet light, and hydrogen peroxide, all of which have previously been shown to cause increased HIV production in cultured human cells. Topically applied arachidonic acid, histamine, ethanol, acetone, and methanol did not increase reporter gene activities.

A lack of published reports on activation of HIV-1 in human cells by these agents suggests that they do not activate **viral** expression in human cells, which corroborates with the findings of this report. Minor forms of skin wounding and intraperitoneally administered psoralen plus ultraviolet light also increased reporter gene activities in skin. Control and test **treatments** could be performed on the same mouse and repetitive samples could be obtained from each **treatment** area. These transgenic mice might be useful as **predictive** models for regulation of the LTR in epidermal or **dendritic** cells.

7/7/28 (Item 28 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07236133 BIOSIS NO.: 000090016007
CELLS WITH DENDRITIC MORPHOLOGY AND BRIGHT INTERLEUKIN-1-ALPHA STAINING CIRCULATE IN THE BLOOD OF PATIENTS WITH RHEUMATOID ARTHRITIS
AUTHOR: BARKLEY D E H; FELDMANN M; MAINI R N
AUTHOR ADDRESS: DIV. CLINICAL IMMUNOLOGY, KENNEDY INST. RHEUMATOLOGY, 6 BUTE GARDENS, LONDON W6 7DW, ENGLAND.
JOURNAL: CLIN EXP IMMUNOL 80 (1). 1990. 25-31. 1990
FULL JOURNAL NAME: Clinical and Experimental Immunology
CODEN: CEXIA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Freshly isolated peripheral blood mononuclear cells (PBMC) from 10 healthy volunteers, 28 patients with rheumatoid arthritis (RA), eight patients with osteoarthritis, and five patients with ankylosing spondylitis were examined for interleukin-1.alpha. (IL-1.alpha.) and interleukin-1.beta. (IL-1.beta.) production using monoclonal antibodies and an indirect immunofluorescent method. In freshly isolated PBMC from healthy controls very few cells were stained for either IL-1 type. All 20 RA patients who were not receiving parenteral gold **therapy** had PBMC staining for IL-1.alpha.. In these patients, up to 7.5% of PBMC showed bright IL-1.alpha. staining (range 1.2-7.5%). No IL-1.beta. staining was seen. These IL-1.alpha.-staining cells had a **dendritic** morphology and the percentage of cells staining **correlated** well with levels of C-reactive protein, an index of **disease** activity in these RA patients. Significantly fewer IL-1.alpha.-staining cells were present in the peripheral blood of RA patients receiving gold **therapy** and in the blood of patients with osteoarthritis and ankylosing spondylitis. These IL-1.alpha.-containing cells, circulating in the blood of RA patients and correlating with **disease** activity have not been previously described. These results support the idea that IL-1.alpha. plays an important role in the pathogenesis of rheumatoid inflammation.

7/7/29 (Item 29 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06885019 BIOSIS NO.: 000089038947
AN IMPROVED MODEL OF RECURRENT HERPETIC EYE **DISEASE** IN MICE
AUTHOR: SHIMELD C; HILL T; BLYTH B; EASTY D
AUTHOR ADDRESS: DEP. OPHTHALMOL., MED. SCI. BUILDING, UNIVERSITY WALK, BRISTOL BS8 1TD, ENGLAND.
JOURNAL: CURR EYE RES 8 (11). 1989. 1193-1206. 1989
FULL JOURNAL NAME: Current Eye Research
CODEN: CEYRD
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Mice were passively immunized with serum containing antibodies to herpes simplex virus type 1 (HSV-1) before inoculation on the cornea with HSV-1 strain McKrae. After such immunization most mice survived and most had normal eyes. When primary infection had subsided, mice with normal eyes were selected and treated with cyclophosphamide, dexamethasone and UV irradiation of the inoculated eye or UV irradiation alone, to reactivate latent virus. After either **treatment** mice developed signs of recurrent infection (virus in eyewashings and recurrent corneal and/or lid **disease**). The incidence of such signs was 17/33 (52%) in mice receiving immunosuppressive drugs and UV irradiation and 19/32 (59%) in mice given UV irradiation alone. In mice **treated** with either stimulus **dendritic** or geographic ulceration of the cornea was seen. These closely resembled the herpetic lesions seen in humans. There was good **correlation** between the pattern and distribution of recurrent corneal **disease** and the distribution of cells containing virus antigens in corneal epithelial sheets. Again, as in humans, the induction of recurrent infection was found to correlate poorly with a rise in the level of serum neutralizing antibody. In mice treated with UV irradiation alone corneal ulcers healed and the eyes returned to normal. By contrast, in mice given immunosuppressive drugs and UV irradiation, the ulceration became more severe and the eyes became opaque and vascularized. The use of passive immunization has greatly improved our previously reported model of recurrent herpetic eye **disease** since it has increased the incidence of mice suitable for the induction of recurrent infection and has increased the incidence of such infection.

7/7/30 (Item 30 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05659702 BIOSIS NO.: 000084008107
THE EFFECTS OF CYCLOSPORIN A ON T LYMPHOCYTE AND DENDRITIC CELL SUB-POPULATIONS IN PSORIASIS
AUTHOR: BAKER B S; GRIFFITHS C E M; LAMBERT S; POWLES A V; LEONARD J N; VALDIMARSSON H; FRY L
AUTHOR ADDRESS: DEP. DERMATOL. RES., ST. MARY'S HOSP., PRAED ST., LONDON W2 1NY, U.K.
JOURNAL: BR J DERMATOL 116 (4). 1987. 503-510. 1987
FULL JOURNAL NAME: British Journal of Dermatology
CODEN: BJDEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Sequential skin biopsies from six patients with severe psoriasis were studied during **treatment** with cyclosporin. Four of the patients clearly completely and the remaining two showed a marked improvement. A subset of **dendritic** cells, HLA-DR+ but lacking the T6 antigen characteristically expressed by Langerhans cells (DR + 6-), was observed in lesional epidermis. They disappeared during **treatment**, before clinical improvement was apparent and at a rate which **correlated** with clearance of psoriasis. These cells were not found in normal or uninvolved psoriatic epidermis and their number in lesional skin appeared to be related to the clinical severity of the **disease**. Total numbers of CD4 and CD8, and HLA-DR+ CD8T cells were substantially reduced in both epidermis and dermis prior to clinical improvement. In contrast, there was generally no decrease in the number of HLA-DR+ CD4 T cells in the epidermis during resolution, whereas these cells were reduced by an average of 68% in the dermis. The beneficial effects of cyclosporin in psoriasis further support the hypothesis that T cells play a central role in the pathogenesis of psoriasis. The cellular changes observed in the skin during cyclosporin treatment may help to elucidate the effects of this drug on immunoregulatory mechanisms in man.

7/7/31 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

12047632 EMBASE No: 2003159316
CME posttest
Cancer Control (CANCER CONTROL) (United States) 2003, 10/2 (179-183)
CODEN: CACOF ISSN: 1073-2748
DOCUMENT TYPE: Journal ; Note
LANGUAGE: ENGLISH

7/7/32 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11957643 EMBASE No: 2003068875
Clinical response after intradermal immature dendritic cell vaccination in metastatic melanoma is associated with immune response to particulate antigen
Smithers M.; O'Connell K.; MacFadyen S.; Chambers M.; Greenwood K.; Boyce A.; Abdul-Jabbar I.; Barker K.; Grimmett K.; Walpole E.; Thomas R.
R. Thomas, University of Queensland, Department of Medicine, Princess Alexandra Hospital, Brisbane, QLD 4102 Australia
AUTHOR EMAIL: rthomas@medicine.pa.uq.edu.au
Cancer Immunology, Immunotherapy (CANCER IMMUNOL. IMMUNOTHER.) (Germany) 01 JAN 2003, 52/1 (41-52)
CODEN: CIIMD ISSN: 0340-7004
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 54

Metastatic melanoma is poorly responsive to **treatment**, and immunotherapeutic approaches are potentially beneficial. **Predictors** of clinical response are needed to identify suitable patients. We sought factors associated with melanoma-specific clinical response following intradermal vaccination with autologous melanoma peptide and particulate hepatitis B antigen (HBsAg)-exposed immature monocyte-derived **dendritic** cells (MDDC). Nineteen patients with metastatic melanoma received a maximum of 8, 2-weekly vaccinations of DC, exposed to HBsAg in addition to autologous melanoma peptides. A further 3 patients received an otherwise identical vaccine that did not include HBsAg. Patients were assessed 1-2 monthly for safety, **disease** volume, and cellular responses to HBsAg and melanoma peptide. There was no significant toxicity. Of 19 patients receiving HBsAg-exposed DC, 9 primed or boosted a cellular response to HBsAg, and 10 showed no HBsAg response. HBsAg-specific responses were associated with in vitro T cell responses to melanoma peptides and to phytohemagglutinin (PHA). Zero out of 10 non-HBsAg-responding and 4/9 HBsAg-responding patients achieved objective melanoma-specific clinical responses or **disease** stabilization - 1 complete and 2 partial responses and 1 case of stable **disease** (P = 0.018). Development of melanoma-specific cellular **immunity** and T cell responsiveness to mitogen were greater in the group of patients responding to HBsAg. Therefore stimulation of an immune response to nominal particulate antigen was necessary when presented by melanoma peptide-exposed immature DC, to achieve clinical responses in metastatic melanoma. Since general immune competence may be a determinant of treatment response, it should be assessed in future trials on DC immunotherapy.

7/7/33 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

11889525 EMBASE No: 2003000598
The effect of diltiazem, a calcium channel blocker, in asthmatic patients [2]
Quintieri F.; D'Ambrosio A.; Bachetoni A.
F. Quintieri, Immunology Laboratory, Istituto Superiore di Sanita, Viale Regina Elena, 299-00161 Rome Italy
AUTHOR EMAIL: quintier@iss.it
British Journal of Clinical Pharmacology (BR. J. CLIN. PHARMACOL.) (United Kingdom) 2002, 54/6 (679-680)
CODEN: BCPHB ISSN: 0306-5251
DOCUMENT TYPE: Journal ; Letter
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 8

7/7/34 (Item 4 from file: 73)

11611443 EMBASE No: 2002183675
Human plasma contains a soluble form of CD86 which is present at elevated levels in some leukaemia patients
Hock B.D.; Patton W.N.; Budhia S.; Mannari D.; Roberts P.; McKenzie J.L.
B.D. Hock, Haematology Research Group, Christchurch School of Medicine, PO Box 4345, Christchurch New Zealand
Leukemia (LEUKEMIA) (United Kingdom) 2002, 16/5 (865-873)
CODEN: LEUKE ISSN: 0887-6924
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 34

Cell surface expression of CD86 (mCD86) provides an important co-stimulatory signal which profoundly influences immune responses. In this report, we investigated the potential presence of a circulating soluble form of CD86 (sCD86) in normal individuals and patients with acute myeloid leukaemia (AML) or B cell chronic lymphocytic leukaemia (B-CLL). Circulating sCD86 was detected in the plasma of all normal individuals (1.04 +/- 0.33 ng/ml, n = 51) and patients analysed. Plasma collected from AML patients in remission (n = 6) contained only low levels of sCD86 but significantly elevated levels (>=2.65 ng/ml, P < 0.0001) were detected in 10/24 AML patients analysed at the time of presentation or relapse. Significantly elevated levels of sCD86 were also detected in 2/17 B-CLL patients. There was no correlation between sCD86 levels and other clinical parameters. RT-PCR analysis demonstrated that normal monocytes and dendritic cells, as well as isolated AML (n = 2) and B-CLL (n = 4) cells, expressed an alternatively spliced transcript of CD86 which encoded a soluble form absent in normal T, B and NK cells. The finding that a proportion of leukaemia patients contain elevated levels of sCD86 and that at least some leukaemic cells express sCD86 transcript suggests a potential role for sCD86 in modulating mCD86 signalling during the malignant process.

7/7/35 (Item 5 from file: 73)

11452997 EMBASE No: 2002023339
Antitumor effects of Flt3 ligand in transplanted murine tumor models
Averbook B.J.; Schuh J.L.; Papay R.; Maliszewski C.
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AUTHOR EMAIL: baverbook@mhmc.org
Journal of Immunotherapy (J. IMMUNOTHER.) (United States) 2002, 25/1

(27-35)
CODEN: JOIME ISSN: 1053-8550
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 24

Administration of Flt3 ligand (FL) to mice causes dendritic and natural killer cells to increase but certain solid tumors to regress. Depending on the particular tumor model used, T cells and natural killer cells have been implicated in the protective immune response induced by FL. The current study examined the effects of FL administration on tumor establishment and progression in metastatic and primary tumor models to correlate anatomic location with immunotherapeutic efficacy. FL mediated significant ($p <= 0.05$) therapeutic activity against pulmonary metastases of the murine MC-38 colon adenocarcinoma, particularly when cytokine administration was initiated before tumor inoculation. However, progressive intraabdominal tumors sometimes were observed even in the relative absence of pulmonary metastases. Significant, although less dramatic, antimetastatic effects were observed with MCA-205 and MCA-102 sarcomas and D5 (B16BL6) melanoma. In contrast, FL was ineffective against subcutaneous MC-38 tumors or against several intracranial tumors. This suggests that besides the administration dose, the efficacy of this cytokine depends on the tumor type and possibly the location of the inoculated tumor. Antitumor activities of FL were abolished by whole-body irradiation (500 cGy) and partially abolished by systemic depletion of CD8, CD4, or natural killer cells. The results indicate that optimization of FL immunotherapy of tumors will require a firmer understanding of the relative contributions of tumor burden, location, immune system requirements, and other factors.

7/7/36 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

11251766 EMBASE No: 2001266596
Vaccines in breast **cancer**
Jager E.; Jager D.; Knuth A.
E. Jager, II. Medizinische Klinik, Hamatologie-Onkologie, Krankenhaus Nordwest, Frankfurt Germany
AUTHOR EMAIL: elke.jaeger@licr.org
Breast (BREAST) (United Kingdom) 2001, 10/SUPPL. 3 (158-160)
CODEN: BREAE ISSN: 0960-9776
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 18

Several antigens recognized by cellular and humoral effectors of the immune system have been identified in breast **cancer**. '**Cancer** /Testis' antigens, e.g. MAGE, NY-ESO-1, CT-7; differentiation antigens, e.g. NY-BR-1, CEA; overexpressed antigens, e.g. p53, HER2/neu, MUC-1, LewisX; and mutational antigens, e.g. p53, represent potential targets for antigen-specific immunotherapy. Clinical vaccine studies, mostly performed in melanoma, and aimed at the induction of antigen-specific CD8+ T cell responses in vivo, have helped to establish sensitive tools for the monitoring of immune responses to the vaccine in vivo and in vitro. Delayed-type hypersensitivity (DTH) reactions observed after intradermal injection of antigenic peptides were found to closely correlate with the induction of antigen-specific CD8+ T cell responses. Cytokines (GM-CSF, IL-2, IL-12) and adjuvants (QS21, IFA, MHC class II restricted helper peptides) have mediated increased CD8+ T cell responses against different antigenic peptides. The site of immunization may have important implications for the quality of immune responses induced. Intradermal and intralymphatic vaccination has led to strong CD8+ T cell responses in vivo, measurable at the immunization site, in metastatic lesions and in the

peripheral blood. Intravenous and subcutaneous vaccination have induced measurable immune responses less frequently. Different strategies of vaccination using dendritic cells loaded with antigenic peptides, proteins or lysates prepared from autologous or allogeneic tumour cells have also led to measurable immune responses in vivo. Results, however, were not superior to vaccination with antigenic peptides alone or combined with adjuvants. Focusing on breast **cancer**, one of the most promising antigens for the design of vaccine studies is the CT-antigen NY-ESO-1, which was identified by the SEREX method. NY-ESO-1 is expressed in approximately 30-50% of breast **cancers**. Spontaneous humoral and cellular immune responses against NY-ESO-1 can be detected in 50% of patients with NY-ESO-1+ tumours. Specific DTH- and CD8+ T cell responses were induced after vaccination with NY-ESO-1 derived peptides alone and combined with GM-CSF in the majority of NY-ESO-1-naive patients. Measurable immune responses that can be correlated with the clinical outcome represent an important prerequisite for any immunotherapeutic intervention in **cancer** immunotherapy. At present, measurable but limited **disease** will teach us about any immediate effects of immunotherapy on **cancer** cells. This will lead the way in the near future to sound and justified adjuvant treatment strategies in the specific immunotherapy of breast **cancer**. (c) 2001 Harcourt Publishers Ltd.

7/7/37 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

11214144 EMBASE No: 2001229945
Amiodarone and cyclophosphamide: Potential for enhanced lung toxicity
Bhagat R.; Sporn T.A.; Long G.D.; Folz R.J.
Dr. R.J. Folz, Duke University Medical Center, Div. Pulmonary/Critical Care Med., Duke Univ. Adult Bone Marrow Transp., Box 2620, Durham, NC 27710 United States
Bone Marrow Transplantation (BONE MARROW TRANSPLANT.) (United Kingdom) 2001, 27/10 (1109-1111)
CODEN: BMTRE ISSN: 0268-3369
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 10

Antineoplastic therapy can be associated with drug-induced lung toxicity. With the increasing use of amiodarone for cardiac dysrhythmias there is an increasing possibility of its combined use with chemotherapies for various malignancies. We report a patient on long-term amiodarone who developed biopsy-proven drug-induced lung toxicity after receiving high-dose cyclophosphamide, at a time-frame much shorter than would have been predicted with cyclophosphamide alone. The potential for enhanced lung toxicity secondary to combination of amiodarone and cyclophosphamide is discussed.

7/7/38 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

11192712 EMBASE No: 2001201967
Regression of human mammary adenocarcinoma by systemic administration of a recombinant gene encoding the hFlex-TRAIL fusion protein
Wu X.; He Y.; Falo L.D. Jr.; Hui K.M.; Huang L.
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Molecular Therapy (MOL. THER.) (United States) 2001, 3/3 (368-374)
CODEN: MTOHC ISSN: 1525-0016

DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 35

The tumor necrosis factor (TNF)-related apoptosis-inducing ligand, TRAIL, is a new member of the TNF family. It can specifically induce apoptosis in a variety of human tumors. To investigate the possibility of employing the TRAIL gene for systemic **cancer** therapy, we constructed a recombinant gene encoding the soluble form of the human Flt3L gene (hFlex) at the 5prime end and the human TRAIL gene at the 3prime end. Such design allows the TRAIL gene product to be secreted into the body circulation. We have also demonstrated that the addition of an isoleucine zipper to the N-terminal of TRAIL greatly enhanced the trimerization of the fusion protein and dramatically increased its anti-tumor activity. The fusion protein reached the level of 16-38 mug/ml in the serum after a single administration of the recombinant gene by hydrodynamic-based gene delivery in mice. A high level of the fusion protein correlated with the regression of a human breast tumor established in SCID mice. No apparent toxicity was observed in the SCID mouse model. In addition, the fusion protein caused an expansion of the dendritic cell population in the C57BL/6 recipient mice, indicating that the hFlex component of the fusion protein was functional. Thus, the hFlex-TRAIL fusion protein may provide a novel approach, with the possible involvement of dendritic cell-mediated anti-**cancer** **immunity**, for the treatment of TRAIL-sensitive tumors.

7/7/39 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

11099918 EMBASE No: 2001119860
Sequential analysis of CD34SUP+ and CD34SUP- cell subsets in peripheral blood and leukapheresis products from breast **cancer** patients mobilized with SCF plus G-CSF and cyclophosphamide
Menendez P.; Prosper F.; Bueno C.; Arbona C.; San Miguel J.F.; Garcia-Conde J.; Sola C.; Homedo J.; Cortes-Funes H.; Orfao A.
A. Orfao, Serv. General de Citometria, Hospital Universitario de Salamanca, Paseo San Vicente 58-182, 37007 Salamanca Spain
Leukemia (LEUKEMIA) (United Kingdom) 2001, 15/3 (430-439)
CODEN: LEUKE ISSN: 0887-6924
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 42

Administration of stem cell factor (SCF) has been proven to enhance cytokine-induced mobilization of CD34SUP+ hematopoietic progenitor cells (HPC) into the peripheral blood (PB). The aim of the present study was to explore in a homogeneous group of 22 uniformly treated breast **cancer** patients: (1) the kinetics of mobilization into PB of both CD34SUP+ and CD34SUP- cell subsets, including dendritic cells, in sequential samples obtained from day + 7 up to day + 12 after mobilization; and (2) the composition of the CD34SUP+ and CD34SUP- cell subsets present in the two leukapheresis products obtained for each patient. The following CD34SUP+ and CD34SUP- subsets were analyzed: early CD34SUP+ HPC, erythroid-, myeloid- and B-lymphoid-committed CD34SUP+ precursor cells, mature T, B and NK cells, monocytes, neutrophils, eosinophils, basophils, and dendritic cells (DC) including three subsets of linSUP-/HLADRSUP+DC (CD16SUP+, CD33SUPhigh and CD123 SUPhigh). Our results show that the absolute number of PB CD34SUP+ HPC progressively increases from day + 7 onwards. As far as the CD34SUP- PB leukocyte subsets are concerned, monocytes (CD14SUP+) displayed the earliest recovery after mobilization predicting neutrophil recovery 1 day in advance. The number of CD34SUP+ HPC collected in a single leukapheresis product was always >=1.4 x 10SUP6 cells/kg body weight. No significant changes were observed between the two leukapheresis sessions

either as regards their composition in CD34SUP+ HPC subsets or their CD34SUP- leukocyte populations except for a higher ratio of both CD34SUP+ erythroid/CD34SUP+ myeloid HPC (0.35 +/- 0.13 vs 0.30 +/- 0.13; P = 0.04) and neutrophils/monocytes (1.58 +/- 2.1 vs 0.69 +/- 0.27; P = 0.009) found for the first leukapheresis. Interestingly, the overall number of dendritic cells (DC) was higher in the second leukapheresis (1.06 +/- 0.56 vs 1.9 +/- 0.46; P = 0.02) due to a selective increase of the CD16SUP+ antigen-presenting cells. In summary, our results show that the combination of cyclophosphamide, G-CSF and SCF is highly effective for stem cell mobilization, with differences observed in the mobilization kinetics of the different hematopoietic cell subsets analyzed.

7/7/40 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

10857671 EMBASE No: 2000338767

In vitro induction of tumor-specific human lymphocyte antigen class I-restricted CD8sup + cytotoxic T lymphocytes by ovarian tumor antigen-pulsed autologous dendritic cells from patients with advanced ovarian **cancer**

Santin A.D.; Hermonat P.L.; Ravaggi A.; Bellone S.; Pecorelli S.; Cannon M.J.; Parham G.P.

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American Journal of Obstetrics and Gynecology (AM. J. OBSTET. GYNECOL.) (United States) 2000, 183/3 (601-609)

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DOCUMENT TYPE: Journal; Article

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 25

OBJECTIVE: The purpose of this study was to evaluate the potential of dendritic cells pulsed with whole-tumor extracts derived from autologous ovarian **cancer** cells in eliciting a tumor-specific cytotoxic T-cell response in vitro from patients with advanced ovarian **cancer**. STUDY DESIGN: CD8sup + T lymphocytes stimulated in vitro with autologous ovarian tumor lysate-pulsed dendritic cells were tested for their ability to induce a human leukocyte antigen class I-restricted cytotoxic T-lymphocyte response able to specifically kill autologous tumor cells in standard 6-hour chromium 51 cytotoxicity assays. In addition, to correlate cytotoxic activity by cytotoxic T-lymphocytes with a particular lymphoid subset, 2-color flow cytometric analysis of intracellular cytokine expression (interferon gamma and interleukin 4) at the single-cell level was performed. RESULTS: Cytotoxic T lymphocytes specific for autologous ovarian tumor cells were elicited from 3 patients with advanced ovarian **cancer**. Although cytotoxic T-lymphocyte populations expressed strong cytolytic activity against autologous tumor cells, they did not lyse concanavalin A-stimulated autologous lymphocytes or autologous Epstein-Barr virus-transformed lymphoblastoid cell lines and showed negligible cytotoxicity against the natural killer cell-sensitive cell line K-562. Cytotoxic effect against the autologous tumor cells was inhibited by an anti-human leukocyte antigen class I monoclonal antibody (W6/32). It is interesting that CD8sup + cytotoxic T lymphocytes expressed variable levels of CD56, a marker that may be associated with high cytotoxic activity. Finally, most of the tumor-specific CD8sup + T cells exhibited a T(H)1 cytokine bias, and a high percentage of interferon gamma expressors among cytotoxic T lymphocytes was **correlated** with higher cytotoxic activity. CONCLUSION: These data show that tumor lysate-pulsed **dendritic** cells can consistently induce in vitro specific CD8sup + cytotoxic T lymphocytes able to kill autologous tumor cells from patients with advanced stage ovarian **cancer**. This novel approach may have

important implications for the **treatment** of residual or resistant **disease** with active or adoptive immunotherapy after standard surgical and cytotoxic treatment.

7/7/41 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

07842130 EMBASE No: 1999088004
Disease modifying treatments for multiple sclerosis: What is on the horizon?
Weilbach F.X.; Gold R.
Dr. F.X. Weilbach, Neurologische Universitatsklinik, Julius-Maximilians-Univ. Wurzburg, Josef-Schneider-Str. 11, D-97080 Wurzburg Germany
AUTHOR EMAIL: f.weilbach@mail.uni-wuerzburg.de
CNS Drugs (CNS DRUGS) (New Zealand) 1999, 11/2 (133-157)
CODEN: CNDRE ISSN: 1172-7047
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 255

Stimulated by the successful introduction of interferon-beta as treatment for relapsing-remitting multiple sclerosis (MS) and based on an improved knowledge of the immunopathology of MS, a vast array of treatment options is currently under investigation for **disease** course modification. These are targeting relapse duration and intensity, relapse rate, **disease** progression and remyelination. The different approaches comprise mostly recombinant biotechnical agents, but also conventional immunosuppressants. Interferon-beta now can be regarded as an established **disease** modifying agent in relapsing remitting and secondary progressive MS as shown unequivocally in several well designed studies conducted by different pharmaceutical companies. Glatiramer acetate is also effective in relapsing remitting MS, although this conclusion is based on a lower level of evidence. A recent positive trial of mitoxantrone in chronic progressive MS underlines the efficacy of immunosuppression at least in subgroups of patients with MS who have high **disease** activity. Aside from the therapeutic approaches now already introduced into the clinical armamentarium, newer agents and treatment concepts include monoclonal antibodies, intravenous immunoglobulins, modulators of trimolecular complex and agents that interact with costimulatory molecules. Cytokine modulators and inhibitors of cell adhesion are promising candidates but their effect on the disturbed immunological network associated with MS has to be investigated thoroughly. In the future, simultaneous or sequential combinations of agents with different targets may significantly improve the efficacy of **treatments** for MS. The clinical evaluation of new **treatment** approaches will be difficult given the hetoregeneity and unpredictable course of the disorder. Interesting future **therapeutic** approaches include intracellular signal transduction modulators, vitamins and newer immunosuppressants. Gene **therapy**, vaccination with naked DNA or **dendritic** cells may also turn out to be useful. Besides developing new immunotherapies it seems indispensable to improve delivery of symptomatic **treatment** and rehabilitation aiming at the quality of life of individual MS patients. Identification of **disease** course **predictors** or **treatment** response will improve accuracy of **therapeutic** decision making.

7/7/42 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

05415361 EMBASE No: 1993183460

Plasticity of the nigrostriatal system in MPTP-treated mice: A biochemical and morphological correlation

Cruz-Sanchez F.F.; Cardozo A.; Ambrosio S.; Tolosa E.; Mahy N.
Biochemistry Unit, School of Medicine, University of Barcelona, Av. Diagonal, 643,08028-Barcelona Spain

Molecular and Chemical Neuropathology (MOL. CHEM. NEUROPATHOL.) (United States) 1993, 19/1-2 (163-176)
CODEN: MCHNE ISSN: 1044-7393
DOCUMENT TYPE: Journal; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

In order to compare the recovery capacity of the nigrostriatal system between adult and old mice, MPTP hydrochloride was administered to 48 BL/C57 male mice, which were sacrificed 24 h or 10 d after the second dose. The animals were divided into four groups, based on age (adult or old) and moment of sacrifice (24 h or 10 d). The detailed morphology of the neurons and the cellular processes of the substantia nigra pars compacta and the striatum were studied using the Golgi method. Immunostaining with a polyclonal glial fibrillary acidic protein antiserum using the peroxidase-antiperoxidase technique was performed to study the glial response. Striatal catecholamines were determined to correlate the biochemical data with the morphological changes. Significant neuronal changes of cellular processes were observed in substantia nigra pars compacta from all MPTP-treated mice, consisting of swelling and distortion of cellular bodies, discontinuous thickness, and nodulations of dendrites with baded aspect. Axons showing focal swelling and nodulations were also found in the neuropil of silver impregnated striata. Marked gliosis with reactive astrocytes in substantia nigra and striatum from all the old treated mice was found. Recovery was only observed in adult mice sacrificed 10 d after withdrawal. At this time, all the old MPTP-**treated** mice showed marked neuronal changes and a persistent marked gliosis. As expected, 24 h after the MPTP **treatment**, a marked depletion of dopamine and its metabolites was found in all the animals; at 10 d, the depletion was partially reversed in the adult group. These data **correlate** well with the observed morphological changes. Our results suggest that, in mice, deterioration of **dendritic** and axonal neuropil constitutes a significant causal factor of the MPTP neurotoxicity. These features are related to the age of the animals and the integrity of the plasticity phenomena, which appear to be altered in old mice.

7/7/43 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

04293619 EMBASE No: 1990176175
Morphological alterations induced by doxorubicin in B16 melanoma cells

Mariani M.; Supino R.
Instituto Nazionale Tumori, Via Venezian 1,20133 Milan Italy

Cancer Letters (CANCER LETT.) (Ireland) 1990, 51/3 (209-212)
CODEN: CALED ISSN: 0304-3835
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

In B16 melanoma, cells morphologically different can be distinguished. In order to establish possible **correlations** between cell morphology and drug-response, the cytotoxic response to doxorubicin was analyzed. The two subpopulations, represented by two types of colonies, showed a different degree of sensitivity to doxorubicin. Moreover, following **treatment**, colonies strongly altered in their morphology were found, suggesting a differentiating activity of doxorubicin (**dendritic** prolongations, increase of intracellular melanin, block of cell proliferation). These results suggest that doxorubicin, besides having a different cytotoxic effect on the two cell subpopulations, induces in this cell line

morphological alterations consistent with a differentiation process.

7/7/44 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

03308811 EMBASE No: 1986016388
Epidermal T lymphocytes and dendritic cells in chronic plaque psoriasis: The effects of PUVA treatment
Baker B.S.; Swain A.F.; Griffiths C.E.M.; et al.
Department of Immunology, St. Mary's Hospital Medical School, London W2 1PG United Kingdom
Clinical and Experimental Immunology (CLIN. EXP. IMMUNOL.) (United Kingdom) 1985, 61/3 (526-534)
CODEN: CEXIA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

The numbers and HLA-DR expression of T cell subsets and dendritic cells in chronic psoriatic plaques were compared to previously reported findings in spontaneously resolving guttate lesions, and the effects of PUVA treatment on these cell populations studied. The chronic lesions showed a similar T helper/T suppressor (T(H)/T(S)) ratio (0.66 +/- 0.10) to resolving guttate lesions. However, in contrast to the resolving lesions which do not contain activated epidermal T(H) cells, a substantial proportion of the T(H) cells in the persistent plaques were DRsup +. Moreover, these persistent lesions contained markedly increased numbers of DRsup + **dendritic** cells, approximately 20% of which were T6 negative. PUVA-induced resolution of chronic lesions was associated with depletion of epidermal T(H) and T(S) cells, and a subsequent reduction in DRsup + **dendritic** cells. In each patient the rate of disappearance of both cell types **correlated** with the rate of resolution. Furthermore, the epidermal T cell depletion preceded the onset of clinical improvement. In contrast, significant reduction of the **dendritic** cells was generally not observed until the lesions were largely resolved. **Dendritic** cells decreased faster in uninvolved than in lesional skin and to a subnormal level. Dermal T cells also decreased during PUVA **therapy** but this did not show any obvious **correlation** with resolution of the lesions. Blood T cell levels were not significantly affected by the **treatment**. These findings support the concept that the initiation and maintenance of the psoriatic process requires activation of T(H) cells in the epidermis via interaction with antigen presenting cells. Furthermore PUVA treatment may clear psoriasis by interfering with such a mechanism through its effects on T lymphocytes.

7/7/45 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE

00217273 EMBASE No: 1974207442
Clinical evaluation of early polyinosinic polycytidylic acid therapy in experimental herpes simplex keratoconjunctivitis
Chowchuvech E.; Sawicki L.; Weissenbacher M.; Galin M.A.
Dept. Ophthalmol., New York Med. Coll., New York, N.Y. 10029 United States
Annals of Ophthalmology (ANN. OPHTHALMOL.) 1974, 6/2 (127-138)
CODEN: ANOPB
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

This study was undertaken to investigate the incidence, chronology and severity of clinical signs in experimental keratoconjunctivitis, their

eventual **correlation** with the kinetics of the major parameters of the infectious process, and the effects of topical polyinosinic polycytidilic acid (In Cn) **treatment** started 1 hr after infection. The **treatment** somewhat reduced the incidence and size of geographic ulcers which peaked on day 8 p.i., but not of punctate and **dendritic** lesions obvious already on day 2. Stromal **disease** appeared on day 8 when also circulating antibody became measurable and its incidence and severity were somewhat reduced among the treated rabbits which produced less circulating antibody. The rate and extent of virus replication in corneal tissues were the same in the treated and control animals. A delay and partial suppression of virus replication was found in the conjunctivas of the treated rabbits. Milder forms of conjunctivitis, obvious by day 5, were not influenced by the treatment but the most severe forms appeared exclusively among untreated rabbits, probably due to the interferon mechanism triggered. This mechanism, as well as a quick removal, from the vascularized conjunctiva, of toxic substances might be responsible for the late appearance of conjunctivitis. The impaired removal of cell decay material from the avascular cornea and lack of evidence for the interferon mechanism being operative, may explain the early appearance of corneal signs. The In Cn treatment had no effect upon the death rates due to encephalitis.

7/7/46 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14912548 22658250 PMID: 12774244

Angiogenesis and dendritic cell density are not correlated with metachronous distant metastasis in curatively operated rectal **cancer**.

Gunther K; Radkow T; Reymond M A; Pfluger R; Dimmler A; Hohenberger W; Papadopoulos T

Department of Surgery, University of Erlangen, Krankenhausstrasse 12, 91054, Erlangen, Germany, Klaus.guenther@rzmail.uni-erlangen.de

International journal of colorectal disease (Germany) 02 08 2003, 18 (4) p300-8, ISSN 0179-1958 Journal Code: 8607899

Document type: Journal Article

Languages: ENGLISH

Main Citation Owner: NLM

Record type: In Process

BACKGROUND AND AIMS. Apart from surgery, treatment of rectal **cancer** increasingly involves the use of (neo-)adjuvant strategies. To optimize the selection process for these therapy regimens, especially in the field of cellular and molecular biology, new prognostic factors additional to the established TNM system are being investigated. PATIENTS AND METHODS. Two groups of patients (n=2x85) with rectal carcinoma curatively treated by surgery alone were studied retrospectively (median follow-up 6.1 years). To exclude the effect of the surgeon only patients free of locally recurrent **disease** were selected. Patient groups were matched for age, gender, UICC stage, and year of operation (1982-1991) and differed only in subsequent metachronous distant metastatic spread, i.e., the criterion to be studied. The factors investigated in uni- and multivariate analysis were angiogenesis, density of **dendritic** cells, grading, venous invasion, and lymphatic invasion. RESULTS. Grading invariably proved to be the only significant prognostic factor. In univariate analysis the absence of venous invasion was also **correlated** significantly with increased **disease**-free survival. CONCLUSION. Angiogenesis and **dendritic** cell density are not prognostic factors for metachronous distant metastasis in rectal **cancer** and therefore cannot serve as selection parameters for adjuvant **therapy**.

Record Date Created: 20030529

7/7/47 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14870248 22635261 PMID: 12750276
Archaeosomes Induce Enhanced Cytotoxic T Lymphocyte Responses to Entrapped Soluble Protein in the Absence of Interleukin 12 and Protect against Tumor Challenge.
Krishnan Lakshmi; Sad Subash; Patel Girishchandra B; Sprott G Dennis
Institute for Biological Sciences, National Research Council of Canada, Ottawa, Ontario, K1A 0R6 Canada.
Cancer research (United States) May 15 2003, 63 (10) p2526-34, ISSN 0008-5472 Journal Code: 2984705R
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
Archaeosome adjuvants formulated as archaeal ether glycerolipid vesicles induce strong CD4(+) as well as CD8(+) CTL responses to entrapped soluble antigens. Immunization of mice with ovalbumin (OVA) entrapped in archaeosomes composed of the total polar lipids of Methanobrevibacter smithii resulted in a potent OVA-specific CD8(+) T-cell response, and subsequently, the mice dramatically resisted solid tumor growth of OVA-expressing EG.7 cells and lung metastasis of B16OVA melanoma cells. Prophylactic protection was antigen-specific because tumor curtailment was not seen in mice injected with antigen-free archaeosomes. Similarly, there was no protection against B16 melanoma cells lacking OVA expression. Furthermore, in vivo depletion of CD8(+) T cells abrogated the protective response, indicating that the antitumor **immunity** was mediated by CTLs. Depletion of CD4(+) T cells also resulted in partial loss of tumor protection, suggesting a beneficial role for T-helper cells. Interestingly OVA-archaeosomes induced enhanced CTL response in the absence of interleukin 12 and IFN-gamma. Furthermore, interleukin 12-deficient mice mounted strong tumor protection. However, IFN-gamma-deficient mice, despite the strong CTL response, were only transiently protected, revealing a need for IFN-gamma response in tumor protection. Archaeosomes also facilitated **therapeutic** protection when injected into mice concurrent with tumor cells. Interestingly, even archaeosomes lacking entrapped antigen mediated **therapeutic** protection, and this **correlated** to the activation of innate **immunity** as evident by the increased tumor-infiltrating natural killer and **dendritic** cells. Thus, archaeosomes represent effective tumor antigen delivery vehicles that can mediate protection by activating both innate as well as acquired **immunity**.
Record Date Created: 20030516

7/7/48 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09768144 21573046 PMID: 11715617
[Angiogenesis and density of dendritic cells do not correlate with metachronous distant metastases after curative surgery of rectal carcinoma]
Angiogenese und Dichte dendritischer Zellen korrelieren nicht mit der metachronen Fernmetastasierung beim kurativ operierten Rectumcarcinom.
Gunther K; Radkow T; Reymond M A; Pfluger R; Dimmler A; Hohenberger W; Papadopoulos T
Chirurgische Klinik mit Poliklinik, Universitat Erlangen-Nurnberg, Erlangen. klaus.guenther@rzmail.uni-erlangen.de
Der Chirurg; Zeitschrift fur alle Gebiete der operativen Medizen (Germany) Oct 2001, 72 (10) p1144-53, ISSN 0009-4722 Journal Code: 16140410R
Document type: Journal Article ; English Abstract
Languages: GERMAN

Main Citation Owner: NLM
Record type: Completed
INTRODUCTION: Besides surgery, treatment of rectal **cancer** increasingly comprises (neo-)adjuvant strategies. To optimise the selection process for these therapy regimens especially in the field of cellular and molecular biology, new prognostic factors besides the established TNM system are being investigated. METHODS: Retrospectively, two groups of patients (n = 2 x 85) with rectal carcinoma curatively treated by surgery alone were studied (median follow-up: 6.1 years). The patients were selected to be free of local **disease**, in order to exclude surgical influence. Patient groups were matched for age, gender, UICC stage and year of operation (1982-1991) and differed only in subsequent metachronous distant metastatic spread, the criterion to be studied. The factors to be investigated in uni- and multivariate analysis were angiogenesis, density of **dendritic** cells, grading, venous and lymphatic invasion. RESULTS: Grading always proved to be the only significant prognostic factor (P < 0.0001). In univariate analysis, absent venous invasion also **correlated** significantly with increased **disease**-free survival (P = 0.0170). CONCLUSIONS: Angiogenesis and density of **dendritic** cells in rectal **cancer** are not prognostic factors for metachronous distant metastasis and, therefore, cannot serve as selection parameters for adjuvant **therapy**.
Record Date Created: 20011121
Record Date Completed: 20020103

7/7/49 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09763086 21567620 PMID: 11709608
Association of clinical, radiological and synovial immunopathological responses to anti-rheumatic treatment in rheumatoid arthritis.
Pettit A R; Weedon H; Ahern M; Zehntner S; Frazer I H; Slavotinek J; Au V ; Smith M D; Thomas R
Centre for Immunology and Cancer Research, University of Queensland, Princess Alexandra Hospital, Brisbane, Queensland, Australia.
Rheumatology (Oxford, England) (England) Nov 2001, 40 (11) p1243-55, ISSN 1462-0324 Journal Code: 100883501
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
OBJECTIVES: To compare immunohistochemical scoring with clinical scoring and radiology for the assessment of rheumatoid arthritis (RA) **disease** activity, synovial tissue (ST) biopsied arthroscopically was assessed from 18 patients before and after commencement of **disease**-modifying anti-rheumatic drug (DMARD) therapy. METHODS: Lymphocytes, macrophages, differentiated dendritic cells (DC), vascularity, tumour necrosis factor (TNF) alpha and interleukin-1beta levels were scored. Clinical status was scored using the American College of Rheumatology (ACR) core set and serial radiographs were scored using the Larsen and Sharp methods. Histopathological evidence of activity included infiltration by lymphocytes, DC, macrophages, tissue vascularity, and expression of lining and sublining TNFalpha. These indices co-varied across the set of ST biopsies and were combined as a synovial activity score for each biopsy. RESULTS: The change in synovial activity with treatment correlated with the ACR clinical response and with decreased radiological progression by the Larsen score. The ACR response to DMARD therapy, the change in synovial activity score and the slowing of radiological progression were each greatest in patients with high initial synovial vascularity. CONCLUSIONS: The data demonstrate an association between clinical, radiological and synovial immunopathological responses to anti-rheumatic treatment in RA. High ST vascularity may predict favourable clinical and radiological

responses to treatment.
Record Date Created: 20011116
Record Date Completed: 20011218

7/7/50 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09170710 20475490 PMID: 11021286
[The efficacy of acyclovir treatment in the therapy of herpetic keratitis]
Eficienta tratamentului cu acyclovir in terapia keratitei herpetice.
Turlea M; Raica D; Haidar A
Spitalul Municipal Arad, Sectia Oftalmologie.
Oftalmologia (Bucharest, Romania - 1990) (ROMANIA) 1999, 49 (4) p55-8, ISSN 1120-0875 Journal Code: 9111247
Document type: Clinical Trial; Journal Article ; English Abstract
Languages: ROMANIAN
Main Citation Owner: NLM
Record type: Completed
There were investigated 51 patients, 19 female and 32 male, with ages between 12 and 80 years, hospitalized in the Dept. Ophthalm. of the City Hospital of Arad, during 1995-1997. From these, 21 had the clinical diagnosis of superficial keratitis, typical form of **dendritic** ulcer, 7 had non-typical forms, and 4 had stromal keratitis; 19 patients recurred. The diagnosis of herpetic keratitis was established **correlating** the clinical aspect with the cytologic examination, made on conjunctivo-corneane smears. A number of 32 patients received a specific **treatment** with Acyclovir, in an ointment form in local applications and on general route orally; there were also associated mydriatics and epitelizants of the cornea. The evolution of the **disease** was evaluated by comparing results obtained in different groups of patients.
Record Date Created: 20001019
Record Date Completed: 20001019

7/7/51 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09165644 20468866 PMID: 11016651
Use of two predictive algorithms of the world wide web for the identification of tumor-reactive T-cell epitopes.
Lu J; Celis E
Department of Immunology and Cancer Center, Mayo Clinic and Mayo Graduate School, Rochester, Minnesota 55905, USA.
Cancer research (UNITED STATES) Sep 15 2000, 60 (18) p5223-7, ISSN 0008-5472 Journal Code: 2984705R
Contract/Grant No.: R01CA80782; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Tumor cells can be effectively recognized and eliminated by CTLs. One approach for the development of CTL-based **cancer** immunotherapy for solid tumors requires the use of the appropriate immunogenic peptide epitopes that are derived from defined tumor-associated antigens. Because CTL peptide epitopes are restricted to specific MHC alleles, to design immune therapies for the general population it is necessary to identify epitopes for the most commonly found human MHC alleles. The identification of such epitopes has been based on MHC-peptide-binding assays that are costly and labor-intensive. We report here the use of two computer-based prediction algorithms, which are readily available in the public domain

(Internet), to identify HL4-B7-restricted CTL epitopes for carcinoembryonic antigen (CEA). These algorithms identified three candidate peptides that we studied for their capacity to induce CTL responses in vitro using lymphocytes from HLA-B7+ normal blood donors. The results show that one of these peptides, CEA9(632) (IPQQHTQVL) was efficient in the induction of primary CTL responses when dendritic cells were used as antigen-presenting cells. These CTLs were efficient in killing tumor cells that express HLA-B7 and produce CEA. The identification of this HLA-B7-restricted CTL epitope will be useful for the design of ethnically unbiased, widely applicable immunotherapies for common solid epithelial tumors expressing CEA. Moreover, our strategy of identifying MHC class I-restricted CTL epitopes without the need of peptide/HLA-binding assays provides a convenient and cost-saving alternative approach to previous methods.
Record Date Created: 20001013
Record Date Completed: 20001013

7/7/52 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

08141644 94207513 PMID: 1364252
Lack of correlation between UV-induced enhancement of melanoma development and local suppression of contact hypersensitivity.
Donawho C K; Kripke M L
Department of Immunology, University of Texas M. D. Anderson Cancer Center, Houston.
Experimental dermatology (DENMARK) Jul 1992, 1 (1) p20-6, ISSN 0906-6705 Journal Code: 9301549
Contract/Grant No.: CA16672; CA; NCI; RO1-CA52457; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Injection of melanoma cells into the UV-irradiated ear skin of syngeneic mice results in an increased incidence of melanomas compared with that in nonirradiated ear skin. This effect of UV is localized to the site of irradiation and appears to be immunologically mediated. In these studies we test the hypothesis that the effect of UV irradiation on melanoma development is related to its ability to alter epidermal Langerhans cells and impair the induction of contact hypersensitivity. A regimen of UV irradiation that altered epidermal immune cells and interfered with the generation of contact hypersensitivity was tested for its ability to increase the incidence of melanoma. Conversely, the ear skin of C3H mice **treated** with a regimen of UV radiation that enhanced melanoma development was examined for the number of appearance of ATPase+ and Thy-1+ **dendritic** epidermal cells and tested for the ability to initiate a contact hypersensitivity response. No **correlation** between these effects of UV irradiation could be detected. Furthermore, implantation of melanoma cells into UV-irradiated ear skin resulted in the generation of systemic **immunity** against subsequent tumor challenge. Therefore, we conclude that the ability of UV irradiation to modify melanoma development is unrelated to its effects on the afferent arm of the contact hypersensitivity response and that enhanced melanoma development is not due to an impairment in the induction of tumor **immunity**.
Record Date Created: 19940513
Record Date Completed: 19940513

7/7/53 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

06494792 90119707 PMID: 2153342

Comparative laboratory diagnosis of experimental herpes simplex keratitis.
Lee S F; Storch G A; Reed C A; Hagerty C M; Pepose J S
Department of Ophthalmology, Washington University School of Medicine, St. Louis, MO 63110.
American journal of ophthalmology (UNITED STATES) Jan 15 1990, 109 (1) p8-12, ISSN 0002-9394 Journal Code: 0370500
Contract/Grant No.: EY07057; EY; NEI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
We compared two commercially available tests, a direct immunofluorescence assay and an enzyme-linked immunosorbent assay (ELISA), to **viral** isolation in tissue culture for the laboratory diagnosis of untreated and partially treated experimental herpes simplex virus keratitis. New Zealand albino rabbits were inoculated bilaterally with herpes simplex virus-1 McKrae strain after corneal scarification. One eye of each rabbit was treated with a 1% trifluorothymidine solution daily, starting on the third day after inoculation. The direct immunofluorescence assay showed lower sensitivity for herpes simplex virus detection than **viral** isolation in tissue culture for both untreated and partially treated eyes. The Herpchek ELISA demonstrated similar sensitivity to tissue culture in detecting herpes simplex virus in untreated eyes. In the treated group, however, the Herpchek ELISA showed a higher percentage of eyes positive for herpes simplex virus than did **viral** isolation in tissue culture. After the initiation of antiviral therapy, eyes that no longer harbor infectious virus that can be isolated in tissue culture may remain herpes simplex virus antigen-positive and thus be more amenable to laboratory diagnosis using the rapid ELISA method.
Record Date Created: 19900215
Record Date Completed: 19900215

7/7/54 (Item 9 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

02432736 77122079 PMID: 190437
[Metaherpetic keratitis clinical and virological findings (author's transl)]
Keratitis metaherpetica -- Klinische und virologische Befunde
Sundmacher R; Neumann-Haefelin D
Klinische Monatsblatter fur Augenheilkunde (GERMANY, WEST) Dec 1976, 169 (6) p728-37, ISSN 0023-2165 Journal Code: 0014133
Document type: Journal Article ; English Abstract
Languages: GERMAN
Main Citation Owner: NLM
Record type: Completed
2,277 specimens from 901 eyes were cultured for herpes simplex virus (HSV). 161 of 391 herpes-**diseased** eyes yielded HSV. The clinico-virological **correlation** led to a simple diagnostic and **therapeutic** scheme which is applicable by the ophthalmologist in his office without virological confirmation: 1. Superficial **viral** herpes (**dendritic** keratitis and allied disorders), HSV-isolating rate 96%. 2. Stromal herpes (disciform edema, different types of interstitial herpetic keratitis), only sporadical findings of HSV in the lacrimal fluid. The rate of virus-recovery increases, however, when an interstitial herpetic keratitis ulcerates. 3. Metaherpetic corneal **disease** = chronic or chronic recurrent superficial postherpetic **disease** without any detectable HSV-activity (main types: metaherpetic erosion, metaherpetic ulcer, metaherpetic bullous keratopathy). One of four superficial herpetic corneal **diseases** proved to be nonviral, i.e. metaherpetic in our series. Metaherpetic **diseases** may be widely considered as a

therapeutic entity. The differential diagnosis with the slitlamp only and the proposed therapy (highly hydrophilic soft lenses plus adequate additional eye drops) are discussed in detail. Being aware of the diagnostic criteria and taking advantage of a combined soft lens therapy the treatment of metaherpetic corneal **disease** is easier and more successful than commonly accepted.
  Record Date Created: 19770415
  Record Date Completed: 19770415
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Set     Items   Description
S1        192   (DENDRITIC)(20N)(THERAP? OR TREAT?)(30N)(CORRELAT? OR PRED-
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S2         96   RD S1 (unique items)
S3          0   S2 AND ATP
S4        459   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
S5         81   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)(10N)(A-
                DD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
S6         44   RD S5 (unique items)
S7         54   S2 AND (DISEASE? OR IMMUNITY OR VIRAL OR BACTERIAL OR CANC-
                ER?)
? s s2 and review?
              96  S2
         3375872  REVIEW?
      S8       3  S2 AND REVIEW?
? t s8/7/all
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? ds

Set     Items   Description
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S2         96   RD S1 (unique items)
S3          0   S2 AND ATP
S4        459   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
S5         81   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)(10N)(A-
            DD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
S6         44   RD S5 (unique items)
S7         54   S2 AND (DISEASE? OR IMMUNITY OR VIRAL OR BACTERIAL OR CANC-
            ER?)
? s s2 and review?
              96  S2
         3375872  REVIEW?
      S8       3  S2 AND REVIEW?
? t s8/7/all

 8/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
(c) 2003 BIOSIS. All rts. reserv.

11809170   BIOSIS NO.: 199900055279
Estrogen-mediated structural and functional synaptic plasticity in the
  female rat hippocampus.
AUTHOR: Woolley Catherine S(a)
AUTHOR ADDRESS: (a)Dep. Neurobiol. and Physiol., Northwest. Univ.,
  Evanston, IL 60208**USA
JOURNAL: Hormones and Behavior  34 (2):p140-148 Oct., 1998
ISSN: 0018-506X
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Light and electron microscopic studies have shown that ovarian
  steroids regulate the density and number of excitatory synaptic inputs to
  hippocampal pyramidal cells in the adult female rat; elevated levels of
  estradiol are associated with a higher density of dendritic spine
  synapses on CA1 pyramidal cells. Electrophysiological analyses indicate
  that these hormone-induced synapses increase hippocampal excitability as
  well as the potential for synaptic plasticity. Importantly,
  correlation of  dendritic spine density and sensitivity to
  synaptic input of individual CA1 pyramidal cells from estradiol-
  treated and control animals suggests that synapses induced by
  estradiol may be a specialized subpopulation that contains primarily the
  NMDA subtype of glutamate receptor. The apparent NMDA receptor
  specificity of these synapses may be key to understanding their
  functional significance. Currently, the behavioral consequences of
  additional spine synapses are unknown. Numerous studies have  aimed at
  correlating hormone-induced changes in hippocampal connectivity with
  differences in hippocampus-dependent spatial learning ability in mazes,
  but the results of these efforts have been equivocal. Anatomical,
  electrophysiological, and behavioral studies of estradiol-mediated
  hippocampal plasticity are reviewed. In conclusion, it is suggested
  that standard behavioral tests of hippocampal function are not sufficient
  to reveal the behavioral consequences of hormone-induced hippocampal
  plasticity. Rather, understanding the behavioral consequences of
  estradiol and progesterone effects on hippocampal connectivity may
  require analysis of the hippocampus' cognitive and spatial information
  processing functions in relation to alternative biologically relevant
  behaviors. A (nonexclusive) proposal that hormone-induced hippocampal
  plasticity may facilitate appropriate prepartum/maternal behavior is
  discussed.
```

8/7/2 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

07842130 EMBASE No: 1999088004
Disease modifying treatments for multiple sclerosis: What is on the horizon?
Weilbach F.X.; Gold R.
Dr. F.X. Weilbach, Neurologische Universitatsklinik, Julius-Maximilians-Univ. Wurzburg, Josef-Schneider-Str. 11, D-97080 Wurzburg Germany
AUTHOR EMAIL: f.weilbach@mail.uni-wuerzburg.de
CNS Drugs (CNS DRUGS) (New Zealand) 1999, 11/2 (133-157)
CODEN: CNDRE ISSN: 1172-7047
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 255

Stimulated by the successful introduction of interferon-beta as treatment for relapsing-remitting multiple sclerosis (MS) and based on an improved knowledge of the immunopathology of MS, a vast array of treatment options is currently under investigation for disease course modification. These are targeting relapse duration and intensity, relapse rate, disease progression and remyelination. The different approaches comprise mostly recombinant biotechnical agents, but also conventional immunosuppressants. Interferon-beta now can be regarded as an established disease modifying agent in relapsing remitting and secondary progressive MS as shown unequivocally in several well designed studies conducted by different pharmaceutical companies. Glatiramer acetate is also effective in relapsing remitting MS, although this conclusion is based on a lower level of evidence. A recent positive trial of mitoxantrone in chronic progressive MS underlines the efficacy of immunosuppression at least in subgroups of patients with MS who have high disease activity. Aside from the therapeutic approaches now already introduced into the clinical armamentarium, newer agents and treatment concepts include monoclonal antibodies, intravenous immunoglobulins, modulators of trimolecular complex and agents that interact with costimulatory molecules. Cytokine modulators and inhibitors of cell adhesion are promising candidates but their effect on the disturbed immunological network associated with MS has to be investigated thoroughly. In the future, simultaneous or sequential combinations of agents with different targets may significantly improve the efficacy of **treatments** for MS. The clinical evaluation of new **treatment** approaches will be difficult given the hetoregeneity and unpredictable course of the disorder. Interesting future **therapeutic** approaches include intracellular signal transduction modulators, vitamins and newer immunosuppressants. Gene **therapy**, vaccination with naked DNA or **dendritic** cells may also turn out to be useful. Besides developing new immunotherapies it seems indispensable to improve delivery of symptomatic **treatment** and rehabilitation aiming at the quality of life of individual MS patients. Identification of disease course **predictors** or **treatment** response will improve accuracy of **therapeutic** decision making.

8/7/3 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

02280872 EMBASE No: 1982012033
Chemotherapy of influenza and herpes virus infections
Oxford J.S.
Div. Viral Products, Nat. Inst. Biol. Standards Contr., London United

Kingdom
Journal of the Royal College of Physicians of London (J. R. COLL. PHYS. LONDON) (United Kingdom) 1981, 15/4 (218-226)
CODEN: RCPJA
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

From the clinical point of view, the last few years have shown the necessity for well-controlled (both clinically and virologically) trials. Many of the poorly controlled earlier trials with herpes infections and idoxuridine, ara-C, ether, ultra-violet light and 2-deoxyglucose have been repeated under more stringent conditions and the compounds have been shown to have marginal or no activity. But a number of antiviral compounds with proven efficacy remain, including amantadine for the prophylaxis and treatment of influenza A virus infections, and intravenous ara-A for the treatment of severe life-threatening herpes infections. Several controlled trials have demonstrated the effectiveness of acyclovir against eye infections caused by herpes viruses, while, in a single controlled trial, PFA has shown effectiveness as a topical ointment against herpes labialis. Combination **therapy** with more than one antiviral compound, or with antivirals and interferon, may be more widely used. Supplementation of trifluorothymidine **treatment** with daily local instillation of two drops of leukocyte interferon containing 3x10sup 7 units/cmsup 3 has resulted in more rapid healing of **dendritic** keratitis and faster cessation of virus shedding. The laboratory systems can therefore **predict** antiviral activity with a reasonable degree of confidence. Clinical trials, in spite of the greater difficulties in organisation and subsequent scientific analysis, can be conducted to a correspondingly high standard to give unequivocal data of efficacy or otherwise.

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? s (dendritic or apc? or antigen(w)present?)(20n)(adoptive or administ?)
           98249  DENDRITIC
           31425  APC?
         1129519  ANTIGEN
         3815635  PRESENT?
           65658  ANTIGEN(W)PRESENT?
           26246  ADOPTIVE
         3228183  ADMINIST?
      S9    4023  (DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE
                  OR ADMINIST?)
? s s9 and review?
            4023  S9
         3375872  REVIEW?
     S10     302  S9 AND REVIEW?
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s (dendritic or apc? or antigen(w)present?)(20n)(adoptive or administ?)
           98249  DENDRITIC
           31425  APC?
         1129519  ANTIGEN
         3815635  PRESENT?
           65658  ANTIGEN(W)PRESENT?
           26246  ADOPTIVE
         3228183  ADMINIST?
      S9    4023  (DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE
                  OR ADMINIST?)
? s s9 and review?
            4023  S9
         3375872  REVIEW?
     S10     302  S9 AND REVIEW?
? rd s10
...examined 50 records  (50)
...examined 50 records  (100)
...examined 50 records  (150)
...examined 50 records  (200)
...examined 50 records  (250)
...examined 50 records  (300)
...completed examining records
     S11     269  RD S10 (unique items)
? s s11 and py=2002
            269  S11
         2234855  PY=2002
     S12      48  S11 AND PY=2002
? rd s12
...completed examining records
     S13      48  RD S12 (unique items)
? t s13/3/all

 13/3/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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13524837   BIOSIS NO.: 200200153658
Induction of tolerance in autoimmune diseases by hematopoietic stem cell
  transplantation: Getting closer to a cure?
AUTHOR: Burt Richard K(a); Slavin Shimon; Burns William H; Marmont Alberto
  M
AUTHOR ADDRESS: (a)Division of Immune Therapy and Autoimmune Disease,
  Northwestern University Medical Center, 320 E Superior, Searle Bldg, Rm
  3-489, Chicago, IL, 60611**USA E-Mail: rburt@nwu.edu
JOURNAL: Blood  99 (3):p768-784 February 1, 2002
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Literature Review
RECORD TYPE: Abstract
LANGUAGE: English


 13/3/2     (Item 1 from file: 73)
DIALOG(R)File  73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

12081832     EMBASE No: 2003192816
  RNA-transfected dendritic cells
  Nair S.; Boczkowski D.
  Dr. S. Nair, Department of Surgery, Duke University Medical Center, Box
  2601, Durham, NC 27710  United States
  AUTHOR EMAIL: s.nair@cgct.duke.edu
  Expert Review of Vaccines ( EXPERT REV. VACCINES ) (United Kingdom)
  2002, 1/4 (507-513)
```

CODEN: ERVXA ISSN: 1476-0584
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 49

13/3/3 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

12005351 EMBASE No: 2003112280
Technology evaluation: DCVax, Northwest biotherapeutics
Knutson K.L.
K.L. Knutson, University of Washington, Tumor Vaccine Group, 1959 NE Pacific Street, Seattle, WA 98195 United States
AUTHOR EMAIL: kknutson@u.washington.edu
Current Opinion in Molecular Therapeutics (CURR. OPIN. MOL. THER.) (United Kingdom) 2002, 4/4 (403-407)
CODEN: CUOTF ISSN: 1464-8431
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 27

13/3/4 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

12000989 EMBASE No: 2003112281
Technology evaluation: APC-80200, Dendreon
Rice A.; Hart D.
D. Hart, Mater Medical Research Institute, Aubigny Place, Raymond Terrace, South Brisbane, QLD 4101 Australia
AUTHOR EMAIL: dhart@mmri.mater.org.au
Current Opinion in Molecular Therapeutics (CURR. OPIN. MOL. THER.) (United Kingdom) 2002, 4/5 (523-527)
CODEN: CUOTF ISSN: 1464-8431
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 37

13/3/5 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

11989445 EMBASE No: 2003100274
HIV immunology better understood and vaccination attempts started
Wahren B.; Landay A.
B. Wahren, Swed. Ctr. for Infect. Dis. Control, Dept. Virology, S-105 21, Stockholm Sweden
AIDS (AIDS) (United Kingdom) 2002, 16/SUPPL. 4 (S85-S88)
CODEN: AIDSE ISSN: 0269-9370
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 29

13/3/6 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

11948537 EMBASE No: 2003060428
A potential role of macrophage activation in the treatment of cancer

Klimp A.H.; De Vries E.G.E.; Scherphof G.L.; Daemen T.
Dr. A.H. Klimp, Dept. of Physiological Chemistry, Groningen Univ. Inst. Drug Explor., University of Groningen, A. Deusinglaan 1, 9713 AV Groningen Netherlands
AUTHOR EMAIL: a.h.klimp@med.rug.nl
Critical Reviews in Oncology/Hematology (CRIT. REV. ONCOL. HEMATOL.) (Ireland) 01 NOV 2002, 44/2 (143-161)
CODEN: CCRHE ISSN: 1040-8428
PUBLISHER ITEM IDENTIFIER: S1040842801002037
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 223

13/3/7 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

11904379 EMBASE No: 2003005970
Clinical immunotherapy for brain tumors
Fecci P.E.; Sampson J.H.
Dr. J.H. Sampson, Department of Neurosurgery, Duke University Medical Center, Durham, NC 27710 United States
AUTHOR EMAIL: samps001@mc.duke.edu
Neuroimaging Clinics of North America (NEUROIMAGING CLIN. NORTH AM.) (United States) 2002, 12/4 (641-664)
CODEN: NCNAE ISSN: 1052-5149
PUBLISHER ITEM IDENTIFIER: S1052514902000278
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 192

13/3/8 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

11900176 EMBASE No: 2003012300
Vaccines and melanoma
MELANOMVAKZINIERUNG
Nestle F.O.
F.O. Nestle, Dermatologische Klinik, Universitatsspital, Gloriasstrasse 31, CH-8091 Zurich Switzerland
AUTHOR EMAIL: nestle@derm.unizh.ch
H+G Zeitschrift fur Hautkrankheiten (H G Z. HAUTKR.) (Germany) 01 DEC 2002, 77/12 (675-678)
CODEN: ZHKRA ISSN: 0301-0481
DOCUMENT TYPE: Journal ; Review
LANGUAGE: GERMAN SUMMARY LANGUAGE: ENGLISH; GERMAN
NUMBER OF REFERENCES: 27

13/3/9 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

11875934 EMBASE No: 2002446490
A role for liposomes in genetic vaccination
Gregoriadis G.; Bacon A.; Caparros-Wanderley W.; McCormack B.
G. Gregoriadis, School of Pharmacy, 29-39 Brunswick Square, London WC1N 1AX United Kingdom
AUTHOR EMAIL: gregoriadis@ulsop.ac.uk
Vaccine (VACCINE) (United Kingdom) 20 DEC 2002, 20/SUPPL. 5 (B1-B9)
CODEN: VACCD ISSN: 0264-410X

PUBLISHER ITEM IDENTIFIER: S0264410X02005145
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 30

13/3/10 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE
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11859065 EMBASE No: 2002431511
Emerging strategies in tumor vaccines
Le Poole I.C.; Gerberi M.A.T.; Kast W.M.
Dr. W.M. Kast, Cardinal Bernardin Cancer Center, Loyola University, Chicago Bldg 112, 2160 South 1st Avenue, Maywood, IL 60153 United States

AUTHOR EMAIL: mkast@lumc.edu
Current Opinion in Oncology (CURR. OPIN. ONCOL.) (United States) 2002, 14/6 (641-648)
CODEN: CUOOE ISSN: 1040-8746
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 91

13/3/11 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11858215 EMBASE No: 2002430222
Dendritic cells in innate immune responses againts HIV
Servet C.; Zitvogel L.; Hosmalin A.
A. Hosmalin, Antigen Present. by Dendritic Cell, Immunology Department, Cochin Institute, 27 rue du Fg St Jacques, 75014 Paris France
AUTHOR EMAIL: hosmalin@cochin.inserm.fr
Current Molecular Medicine (CURR. MOL. MED.) (Netherlands) 2002, 2/8 (739-756)
CODEN: CMMUB ISSN: 1566-5240
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 205

13/3/12 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11852425 EMBASE No: 2002427223
Nasopharyngeal carcinoma and the EBV-specific T cell response: Prospects for immunotherapy
Lee S.P.
S.P. Lee, Can. Res. UK Inst. for Can. Studies, University of Birmingham, Edgbaston, Birmingham B15 2TT United Kingdom
AUTHOR EMAIL: leesp@divcs-ex1.bham.ac.uk
Seminars in Cancer Biology (SEMIN. CANCER BIOL.) (United Kingdom) 2002, 12/6 (463-471)
CODEN: SECBE ISSN: 1044-579X
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 64

13/3/13 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

11821681 EMBASE No: 2002393432
Vaccines in the treatment of multiple myeloma
VAKCINY V LEC(caron)BE MNOHOC(caron)ETNEHO MYELOMU
Buchler T.; Musilova R.; Kovar(caron)ova L.; Hajek R.
T. Buchler, Interni Hematoonkol. Klin., Fakultni Nemocnice, Jihlavska 20, 639 00 Brno Czech Republic
AUTHOR EMAIL: buchler@fnbrno.cz
Klinicka Onkologie (KLIN. ONKOL.) (Czech Republic) 2002, 15/SUPPL. (44-47)
CODEN: KLONE ISSN: 0862-495X
DOCUMENT TYPE: Journal ; Short Survey
LANGUAGE: CZECH SUMMARY LANGUAGE: ENGLISH; CZECH
NUMBER OF REFERENCES: 47

13/3/14 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

11804631 EMBASE No: 2002377014
Dendritic cell gene therapy
Onaitis M.; Kalady M.F.; Pruitt S.; Tyler D.S.
Dr. D.S. Tyler, Department of Surgery, Surgical Oncology Section, Duke University Medical Center, Durham, NC 27710 United States
AUTHOR EMAIL: tyler002@acpub.duke.edu
Surgical Oncology Clinics of North America (SURG. ONCOL. CLIN. NORTH AM.) (United States) 2002, 11/3 (645-660)
CODEN: SOCAF ISSN: 1055-3207
PUBLISHER ITEM IDENTIFIER: S1055320702000273
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 53

13/3/15 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

11790060 EMBASE No: 2002347496
Treating human autoimmune disease by depleting B cells
Looney R.J.
Prof. R.J. Looney, University of Rochester, 601 Elmwood Avenue, Rochester, NY 14642 United States
AUTHOR EMAIL: John Looney@URMC.Rochester.edu
Annals of the Rheumatic Diseases (ANN. RHEUM. DIS.) (United Kingdom) 2002, 61/10 (863-866)
CODEN: ARDIA ISSN: 0003-4967
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 40

13/3/16 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE

11777809 EMBASE No: 2002351139
Real-time monitoring of immune responses
Wieder E.D.
E.D. Wieder, Dept. of Blood/Marrow Transplant., University of Texas, MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030 United States

Cytotherapy (CYTOTHERAPY) (United Kingdom) 2002, 4/4 (347-352)
CODEN: CYTRF ISSN: 1465-3249
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

13/3/17 (Item 16 from file: 73)
DIALOG(R)File 73:EMBASE
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11777805 EMBASE No: 2002351135
Universal tumor antigens as targets for immunotherapy
Gordan J.D.; Vonderheide R.H.
R.H. Vonderheide, Abramson Family Cancer Res. Inst., University of Pennsylvania, School of Medicine, 421 Curie Blvd., Philadelphia, PA 19104 United States
Cytotherapy (CYTOTHERAPY) (United Kingdom) 2002, 4/4 (317-327)
CODEN: CYTRF ISSN: 1465-3249
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 87

13/3/18 (Item 17 from file: 73)
DIALOG(R)File 73:EMBASE
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11753333 EMBASE No: 2002328968
STI and beyond: The prospects of boosting anti-HIV immune responses
Allen T.M.; Kelleher A.D.; Zaunders J.; Walker B.D.
T.M. Allen, Massachusetts General Hospital, Division of AIDS, Harvard Medical School, Boston, MA United States
AUTHOR EMAIL: tallen2@partners.org
Trends in Immunology (TRENDS IMMUNOL.) (United Kingdom) 01 SEP 2002, 23/9 (456-460)
CODEN: TIRMA ISSN: 1471-4906
PUBLISHER ITEM IDENTIFIER: S1471490602022974
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 63

13/3/19 (Item 18 from file: 73)
DIALOG(R)File 73:EMBASE
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11749650 EMBASE No: 2002322954
Travels along the viral-immunobiology highway
Oldstone M.B.A.
Prof. M.B.A. Oldstone, Department of Neuropharmacology, Division of Virology, Scripps Research Institute, 10550 North Torrey Pines Road, San Diego, CA 92037 United States
AUTHOR EMAIL: mbaobo@scripps.edu
Immunological Reviews (IMMUNOL. REV.) (United Kingdom) 2002, 185/- (54-68)
CODEN: IMRED ISSN: 0105-2896
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 57

13/3/20 (Item 19 from file: 73)
DIALOG(R)File 73:EMBASE

11731395 EMBASE No: 2002302356
State-of-the-art treatment of metastatic hormone-refractory prostate cancer
Goodin S.; Rao K.V.; DiPaola R.S.
Dr. R.S. DiPaola, Cancer Institute of New Jersey, 195 Little Albany Street, New Brunswick, NJ 08901 United States
AUTHOR EMAIL: dipaolrs@umdnj.edu
Oncologist (ONCOLOGIST) (United States) 2002, 7/4 (360-370)
CODEN: OCOLF ISSN: 1083-7159
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 87

13/3/21 (Item 20 from file: 73)
DIALOG(R)File 73:EMBASE

11686595 EMBASE No: 2002259577
Dendritic cells
Yao V.; Platell C.; Hall J.C.
Prof. J.C. Hall, University Department of Surgery, Royal Perth Hospital, Wellington Street, Perth, WA 6000 Australia
AUTHOR EMAIL: jchall@cyllene.uwa.edu.au
ANZ Journal of Surgery (ANZ J. SURG.) (Australia) 2002, 72/7 (501-506)
CODEN: AJSNB ISSN: 1445-1433
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 50

13/3/22 (Item 21 from file: 73)
DIALOG(R)File 73:EMBASE

11674230 EMBASE No: 2002247582
Clinical trials with CMV-specific T cells
Peggs K.S.; Mackinnon S.
K.S. Peggs, Department of Haematology, University College Hospital, 98 Chenies Mews, London WC1E 6HX United Kingdom
Cytotherapy (CYTOTHERAPY) (United Kingdom) 2002, 4/1 (21-28)
CODEN: CYTRF ISSN: 1465-3249
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 43

13/3/23 (Item 22 from file: 73)
DIALOG(R)File 73:EMBASE

11674228 EMBASE No: 2002247580
Adoptive transfer of Ag-specific T cells to prevent CMV disease after allogeneic stem-cell transplantation
Van Rhee F.; Barrett J.
F. Van Rhee, Myeloma Inst. for Res. and Therapy, Univ. of Arkansas for Med. Sciences, Slot 776, 4301 West Markham, Little Rock, AR 72205 United States
Cytotherapy (CYTOTHERAPY) (United Kingdom) 2002, 4/1 (3-10)
CODEN: CYTRF ISSN: 1465-3249
DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 62

13/3/24 (Item 23 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11670855 EMBASE No: 2002242712
Therapeutic cancer vaccines on trial
Reichert J.M.; Paquette C.
J.M. Reichert, Tufts Ctr. for Stud. of Drug Devmt., Boston, MA United States
AUTHOR EMAIL: janice.reichert@tufts.edu
Nature Biotechnology (NAT. BIOTECHNOL.) (United States) 2002, 20/7 (659-663)
CODEN: NABIF ISSN: 1087-0156
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 11

13/3/25 (Item 24 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11663256 EMBASE No: 2002235136
Cancer immunotherapy with peptide-based vaccines: What have we achieved? Where are we going?
Parmiani G.; Castelli C.; Dalerba P.; Mortarini R.; Rivoltini L.; Marincola F.M.; Anichini A.
Dr. G. Parmiani, Unit of Immunotherapy of Hum. Tumors, Ist. Nazionale Studio Cura Tumori, Via Venezian 1, 20133 Milan Italy
AUTHOR EMAIL: parmiani@istitutotumori.mi.it
Journal of the National Cancer Institute (J. NATL. CANCER INST.) (United Kingdom) 05 JUN 2002, 94/11 (805-818)
CODEN: JNCIA ISSN: 0027-8874
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 148

13/3/26 (Item 25 from file: 73)
DIALOG(R)File 73:EMBASE
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11646330 EMBASE No: 2002218128
Dendritic cells: Immune regulators in health and disease
Lipscomb M.F.; Masten B.J.
M.F. Lipscomb, Dept. of Pathology, BMSB, 915 Camino de Salud NE, Albuquerque, NM 87131-5301 United States
AUTHOR EMAIL: mlipscomb@salud.unm.edu
Physiological Reviews (PHYSIOL. REV.) (United States) 2002, 82/1 (97-130)
CODEN: PHREA ISSN: 0031-9333
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 397

13/3/27 (Item 26 from file: 73)
DIALOG(R)File 73:EMBASE
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11621920 EMBASE No: 2002194722
Immunotherapy for pancreatic cancer: Current concepts
Kaufman H.L.; Di Vito Jr. J.; Horig H.
Dr. H.L. Kaufman, Department of Surgery, Albert Einstein College of Medicine, 1300 Morris Park Avenue, Bronx, NY 10461 United States
AUTHOR EMAIL: kaufman@aecom.yu.edu
Hematology/Oncology Clinics of North America (HEMATOL. ONCOL. CLIN. NORTH AM.) (United States) 2002, 16/1 (159-197)
CODEN: HCNAE ISSN: 0889-8588
PUBLISHER ITEM IDENTIFIER: S0889858801000028
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 179

13/3/28 (Item 27 from file: 73)
DIALOG(R)File 73:EMBASE

11605735 EMBASE No: 2002179002
Dendritic cell-based immunoregulatory strategies
Matsue H.; Kusuhara M.; Matsue K.; Takashima A.
Dr. H. Matsue, Department of Dermatology, Univ. Texas Southwestern Med. Ctr., 5323 Harry Hines Boulevard, Dallas, TX 75390-6069 United States
AUTHOR EMAIL: hiroyuki.matsue@utsouthwestern.edu
International Archives of Allergy and Immunology (INT. ARCH. ALLERGY IMMUNOL.) (Switzerland) 2002, 127/4 (251-258)
CODEN: IAAIE ISSN: 1018-2438
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 87

13/3/29 (Item 28 from file: 73)
DIALOG(R)File 73:EMBASE

11596059 EMBASE No: 2002167944
Immunotherapy of ovarian cancer
Kirby T.O.; Huh W.; Alvarez R.
Dr. R. Alvarez, University of Alabama, Division of Gynecologic Oncology, 618 20th Street South, Birmingham, AL 35233 United States
AUTHOR EMAIL: rdalvarez@aol.com
Expert Opinion on Biological Therapy (EXPERT OPIN. BIOL. THER.) (United Kingdom) 2002, 2/4 (409-417)
CODEN: EOBTA ISSN: 1471-2598
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 65

13/3/30 (Item 29 from file: 73)
DIALOG(R)File 73:EMBASE

11596058 EMBASE No: 2002167943
Prostate-specific antigen vaccines for prostate cancer
Horig H.; Lee C.S.D.; Kaufman H.L.
Dr. H.L. Kaufman, Columbia Presbyterian Medical Center, MHB 7-SK, 177 Fort Washington Avenue, New York, NY 10032 United States
AUTHOR EMAIL: hlk2003@columbia.edu
Expert Opinion on Biological Therapy (EXPERT OPIN. BIOL. THER.) (United Kingdom) 2002, 2/4 (395-408)
CODEN: EOBTA ISSN: 1471-2598

DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 104

13/3/31 (Item 30 from file: 73)
DIALOG(R)File 73:EMBASE

11592500 EMBASE No: 2002163569
Immunotherapy of hepatocellular carcinoma
Butterfield L.H.; Ribas A.
Dr. L.H. Butterfield, UCLA Medical Center, Department of Surgery, Division of Surgical Oncology, Los Angeles, CA 90095 United States
AUTHOR EMAIL: lbutterfield@mednet.ucla.edu
Expert Opinion on Biological Therapy (EXPERT OPIN. BIOL. THER.) (United Kingdom) 2002, 2/2 (123-133)
CODEN: EOBTA ISSN: 1471-2598
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 135

13/3/32 (Item 31 from file: 73)
DIALOG(R)File 73:EMBASE

11588833 EMBASE No: 2002160735
Chronic phase CML patients posses T cells capable of recognising autologous tumour cells
Muller L.; Pawelec G.
L. Muller, Tubingen Ageing/Tumour Immunol. Grp., Section for Transplant. Immunology, Univ. of Tubingen Medical Sch., Tubingen Germany
AUTHOR EMAIL: ludmila.mueller@uni-tuebingen.de
Leukemia and Lymphoma (LEUK. LYMPHOMA) (United Kingdom) 2002, 43/5 (943-951)
CODEN: LELYE ISSN: 1042-8194
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 56

13/3/33 (Item 32 from file: 73)
DIALOG(R)File 73:EMBASE

11565515 EMBASE No: 2002136773
Vaccination against the HER-2/neu oncogenic protein
Bernhard H.; Salazar L.; Schiffman K.; Smorlesi A.; Schmidt B.; Knutson K.L.; Disis M.L.
M.L. Disis, Box 356527, University of Washington, Seattle, WA 98195-6527 United States
AUTHOR EMAIL: ndisis@u.washington.edu
Endocrine-Related Cancer (ENDOCR.-RELAT. CANCER) (United Kingdom) 2002, 9/1 (33-44)
CODEN: ERCAE ISSN: 1351-0088
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 80

13/3/34 (Item 33 from file: 73)
DIALOG(R)File 73:EMBASE

11555418 EMBASE No: 2002128064
Hematopoietic growth factors, dendritic cell biology, and vaccine therapy of cancer
Fay J.W.
Dr. J.W. Fay, Immunologic Therapy for Cancer, Baylor Inst. for Immunology Research, Baylor University Medical Center, 3409 Worth Street, Dallas, TX 75247 United States
AUTHOR EMAIL: jw.fay@baylordallas.edu
Current Opinion in Hematology (CURR. OPIN. HEMATOL.) (United States) 2002, 9/3 (202-206)
CODEN: COHEF ISSN: 1065-6251
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

13/3/35 (Item 34 from file: 73)
DIALOG(R)File 73:EMBASE

11510788 EMBASE No: 2002083163
Immunocytotherapy
Homann D.
D. Homann, Division of Virology, Department of Neuropharmacology, Scripps Research Institute, 10550 North Torrey Pines Road, San Diego, CA 92037 United States
Current Topics in Microbiology and Immunology (CURR. TOP. MICROBIOL. IMMUNOL.) (Germany) 2002, 263/- (43-65)
CODEN: CTMIA ISSN: 0070-217X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 120

13/3/36 (Item 35 from file: 73)
DIALOG(R)File 73:EMBASE

11501086 EMBASE No: 2002072730
The biological treatment of renal-cell carcinoma and melanoma
Nathan P.D.; Eisen T.G.
Dr. T.G. Eisen, Royal Marsden Hospital, Fulham Road, London SW3 6JJ United Kingdom
AUTHOR EMAIL: teisen@icr.ac.uk
Lancet Oncology (LANCET ONCOL.) (United States) 2002, 3/2 (89-96)
CODEN: LOANB ISSN: 1470-2045
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 88

13/3/37 (Item 36 from file: 73)
DIALOG(R)File 73:EMBASE

11470237 EMBASE No: 2002042503
Novel immunotherapies for psoriasis
Asadullah K.; Volk H.-D.; Sterry W.
K. Asadullah, Research Business Area Dermatology, Schering AG, D-13342 Berlin Germany
AUTHOR EMAIL: khusru.asadullah@schering.de
Trends in Immunology (TRENDS IMMUNOL.) (United Kingdom) 01 JAN 2002, 23/1 (47-53)

CODEN: TIRMA ISSN: 1471-4906
PUBLISHER ITEM IDENTIFIER: S1471490601021196
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 46

13/3/38 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14749932 22315946 PMID: 12428910
Antigen delivery to mucosa-associated lymphoid tissues using liposomes as a carrier.
Zho Fan; Neutra Marian R
Department of Pathology, Creighton University School of Medicine, Omaha, NE 68131, USA. fzhou@pathology.creighton.edu
Bioscience reports (United States) Apr **2002**, 22 (2) p355-69, ISSN 0144-8463 Journal Code: 8102797
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

13/3/39 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14749931 22315945 PMID: 12428909
Liposomal delivery of CTL epitopes to dendritic cells.
Chikh Ghania; Schutze-Redelmeier Marie-Paule
British Columbia Cancer Research Center, Dept of Advanced Therapeutics, Vancouver, Canada.
Bioscience reports (United States) Apr **2002**, 22 (2) p339-53, ISSN 0144-8463 Journal Code: 8102797
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

13/3/40 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14749930 22315944 PMID: 12428908
Delivery of protein antigens to the immune system by fusion-active virosomes: a comparison with liposomes and ISCOMs.
Bungener Laura; Huckriede Anke; Wilschut Jan; Daemen Toos
Department of Medical Microbiology, University of Groningen, The Netherlands.
Bioscience reports (United States) Apr **2002**, 22 (2) p323-38, ISSN 0144-8463 Journal Code: 8102797
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

13/3/41 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14604040 22340492 PMID: 12454705
Ovarian follicular lymphoma: a case report and **review** of the literature.
Niitsu Nozomi; Nakamine Hirokazu; Hayama Miyuki; Unno Yumi; Nakamura Shigeo; Horie Ryouichi; Iwabuchi Keiichi; Nakamura Naoya; Miura Ikuo; Higashihara Masaaki
Department of Internal Medicine IV, Kitasato University School of Medicine, 1-15-1 Kitasato, Sagamihara-shi, Kanagawa, 228-8555, Japan. nniitsu@med.kitasato-u.ac.jp
Annals of hematology (Germany) 10 12 **2002**, 81 (11) p654-8, ISSN 0939-5555 Journal Code: 9107334
Document type: Journal Article; Review; Review of Reported Cases
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

13/3/42 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10120478 22089965 PMID: 12094697
[Recent advances in the diagnosis and treatment of colorectal cancers]
Mimori Koshi; Mori Masaki
Department of Surgery, Medical Institute of Bioregulation, Kyushu University, Beppu, Japan.
Nippon Geka Gakkai zasshi (Japan) Jun **2002**, 103 (6) p468-71, ISSN 0301-4894 Journal Code: 0405405
Document type: Journal Article ; English Abstract
Languages: JAPANESE
Main Citation Owner: NLM
Record type: Completed

13/3/43 (Item 6 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

10002806 21931174 PMID: 11934227
Targeting vaccines to dendritic cells.
Foged Camilla; Sundblad Anne; Hovgaard Lars
Department of Pharmaceutics, The Royal Danish School of Pharmacy, Copenhagen. cfo@dfh.dk
Pharmaceutical research (United States) Mar **2002**, 19 (3) p229-38, ISSN 0724-8741 Journal Code: 8406521
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

13/3/44 (Item 7 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09986372 21912715 PMID: 11915941
Immunotherapy against antigenic tumors: a game with a lot of players.
Perez-Diez A; Marincola F M
Surgery Branch, National Cancer Institute, Bethesda, Maryland 20892, USA.
Cellular and molecular life sciences - CMLS (Switzerland) Feb **2002**, 59 (2) p230-40, ISSN 1420-682X Journal Code: 9705402
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM

Record type: Completed

13/3/45 (Item 8 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09871760 21686941 PMID: 11829278
Immune dysfunction in cancer patients.
Carbone Joyce E; Ohm David P
Department of Medicine, Vanderbilt-Ingram Cancer Center, Vanderbilt University Medical Center, Nashville, Tennessee 37232, USA.
Oncology (Williston Park, N.Y.) (United States) Jan **2002**, 16 (1 Suppl 1) p11-8, ISSN 0890-9091 Journal Code: 8712059
Contract/Grant No.: CA76321; CA; NCI; CA81101; CA; NCI
Comment in Oncology (Huntingt). 2002 Jan;16(1 Suppl 1) 7-9; Comment in PMID 11829282
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

13/3/46 (Item 1 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

138071365 CA: 138(6)71365b JOURNAL
Specific deletion of autoreactive T cells by adenovirus-transfected, Fas ligand-producing antigen-presenting cells
AUTHOR(S): Zhang, Huang-Ge; Mountz, John D.; Fleck, Martin; Zhou, Tong; Hsu, Hui-Chen
LOCATION: Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, USA
JOURNAL: Immunol. Res. (Immunologic Research) DATE: 2002 VOLUME: 26 NUMBER: 1-3 PAGES: 235-246 CODEN: IMRSEB ISSN: 0257-277X LANGUAGE: English PUBLISHER: Humana Press Inc.

13/3/47 (Item 2 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

137045538 CA: 137(4)45538v JOURNAL
Dendritic cell maturation in active immunotherapy strategies
AUTHOR(S): Morse, Michael A.; Mosca, Paul J.; Clay, Timothy M.; Lyerly, H. Kim
LOCATION: Department of Medicine and Surgery, Duke University Medical Center, Durham, NC, 2771, USA
JOURNAL: Expert Opin. Biol. Ther. (Expert Opinion on Biological Therapy) DATE: 2002 VOLUME: 2 NUMBER: 1 PAGES: 35-43 CODEN: EOBTA2 ISSN: 1471-2598 LANGUAGE: English PUBLISHER: Ashley Publications Ltd.

13/3/48 (Item 3 from file: 399)
DIALOG(R)File 399:CA SEARCH(R)

136323539 CA: 136(21)323539d JOURNAL
Improvement of adoptive cellular immunotherapy of human cancer using Ex-vivo gene transfer
AUTHOR(S): Paul, Stephane; Calmels, Bastien; Acres, R. Bruce
LOCATION: Clinical and Experimental Immunology Laboratory, Transgene S.A., 67082, Strasbourg, Fr.

JOURNAL: Curr. Gene Ther. DATE: 2002 VOLUME: 2 NUMBER: 1 PAGES: 91-100 CODEN: CGTUAH ISSN: 1566-5232 LANGUAGE: English PUBLISHER: Bentham Science Publishers Ltd.

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? ds

Set     Items   Description
S1        192   (DENDRITIC)(20N)(THERAP? OR TREAT?)(30N)(CORRELAT? OR PRED-
                ICT?)
S2         96   RD S1 (unique items)
S3          0   S2 AND ATP
S4        459   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
S5         81   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)(10N)(A-
                DD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
S6         44   RD S5 (unique items)
S7         54   S2 AND (DISEASE? OR IMMUNITY OR VIRAL OR BACTERIAL OR CANC-
                ER?)
S8          3   S2 AND REVIEW?
S9       4023   (DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE OR
                ADMINIST?)
S10       302   S9 AND REVIEW?
S11       269   RD S10 (unique items)
S12        48   S11 AND PY=2002
S13        48   RD S12 (unique items)
? s s11 and py=2003
             269  S11
          624460  PY=2003
    S14       29  S11 AND PY=2003
? rd s14
...completed examining records
    S15       29  RD S14 (unique items)
? t s15/3all
>>>"3ALL" is not a valid format name in file(s): 5, 73, 155, 399
? t s15/3/all

 15/3/1     (Item 1 from file: 73)
DIALOG(R)File  73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

12096586     EMBASE No: 2003208258
  Gateways to clinical trials
  Bayes M.; Rabasseda X.; Prous J.R.
  M. Bayes, Prous Science, S.A., P.O. Box 540, 08080 Barcelona  Spain
  AUTHOR EMAIL: mbayes@prous.com
  Methods and Findings in Experimental and Clinical Pharmacology ( METHODS
  FIND. EXP. CLIN. PHARMACOL. ) (Spain)   2003, 25/3 (225-248)
  CODEN: MFEPD   ISSN: 0379-0355
  DOCUMENT TYPE: Journal ; Review
  LANGUAGE: ENGLISH   SUMMARY LANGUAGE: ENGLISH
  NUMBER OF REFERENCES: 152


 15/3/2     (Item 2 from file: 73)
DIALOG(R)File  73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

12075378     EMBASE No: 2003187289
  Melanoma vaccines: Early progress and future promises
  Zarour H.M.; Kirkwood J.M.
  Dr. H.M. Zarour, Univ. of Pittsburgh Cancer Institute, Hillman Cancer
  Center, Research Pavilion, 5117 Center Ave, Pittsburgh, PA 15213  United
  States
  AUTHOR EMAIL: zarourhm@msx.upmc.edu
  Seminars in Cutaneous Medicine and Surgery ( SEMIN. CUTANEOUS MED. SURG.
  ) (United States)   2003, 22/1 (68-75)
```

CODEN: SCMSF ISSN: 1085-5629
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 46

15/3/3 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

12072258 EMBASE No: 2003183380
Dendritic cells and HCMV cross-presentation
Arrode G.; Davrinche C.
C. Davrinche, INSERM U 395, CHU Purpan, BP 3028, 31024 Toulouse Cedex France
Current Topics in Microbiology and Immunology (CURR. TOP. MICROBIOL. IMMUNOL.) (Germany) 2003, 276/- (277-294)
CODEN: CTMIA ISSN: 0070-217X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 63

15/3/4 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

12072256 EMBASE No: 2003183378
Viral vectors for dendritic cell-based immunotherapy
Humrich J.; Jenne L.
L. Jenne, Department of Dermatology, University of Erlangen, Hartmannstrasse 14, 91052 Erlangen Germany
Current Topics in Microbiology and Immunology (CURR. TOP. MICROBIOL. IMMUNOL.) (Germany) 2003, 276/- (241-259)
CODEN: CTMIA ISSN: 0070-217X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 89

15/3/5 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

12072254 EMBASE No: 2003183376
Dendritic cell vaccination and viral infection - Animal models
Ludewig B.
B. Ludewig, Institute of Experimental Immunology, Department of Pathology, University of Zurich, Schmelzbergstr. 12, 8091 Zurich Switzerland
Current Topics in Microbiology and Immunology (CURR. TOP. MICROBIOL. IMMUNOL.) (Germany) 2003, 276/- (199-214)
CODEN: CTMIA ISSN: 0070-217X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 79

15/3/6 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

12072253 EMBASE No: 2003183375
Dendritic cell-based immunotherapy

Berger T.G.; Schultz E.S.
E.S. Schultz, Department of Dermatology, University of Erlangen, Hartmannstrasse 14, 91052 Erlangen Germany
Current Topics in Microbiology and Immunology (CURR. TOP. MICROBIOL. IMMUNOL.) (Germany) 2003, 276/- (163-197)
CODEN: CTMIA ISSN: 0070-217X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 165

15/3/7 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

12069375 EMBASE No: 2003174818
Immunotherapy of malignant melanoma
Kadison A.S.; Morton D.L.
Dr. D.L. Morton, John Wayne Cancer Institute, 2200 Santa Monica Boulevard, Santa Monica, CA 90404 United States
AUTHOR EMAIL: mortond@jwci.org
Surgical Clinics of North America (SURG. CLIN. NORTH AM.) (United States) 01 APR 2003, 83/2 (343-370)
CODEN: SCNAA ISSN: 0039-6109
PUBLISHER ITEM IDENTIFIER: S0039610902001627
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 153

15/3/8 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

12051255 EMBASE No: 2003161016
Live recombinant vectors for AIDS vaccine development
Voltan R.; Robert-Guroff M.
M. Robert-Guroff, National Institutes of Health, National Cancer Institute, Basic Research Laboratory, 41 Library Drive, Building 41, Bethesda, MD 20892-5055 United States
AUTHOR EMAIL: guroffm@exchange.nih.gov
Current Molecular Medicine (CURR. MOL. MED.) (Netherlands) 2003, 3/3 (273-284)
CODEN: CMMUB ISSN: 1566-5240
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 140

15/3/9 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

12051252 EMBASE No: 2003161013
Dendritic cells as a conduit to improve HIV vaccines
Pope M.
M. Pope, Center for Biomedical Research, Population Council, 1230 York Avenue, New York, NY 10021 United States
AUTHOR EMAIL: mpope@popcbr.rockefeller.edu
Current Molecular Medicine (CURR. MOL. MED.) (Netherlands) 2003, 3/3 (229-242)
CODEN: CMMUB ISSN: 1566-5240
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

NUMBER OF REFERENCES: 228

15/3/10 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

12048751 EMBASE No: 2003160963
Dendritic cell-based immunotherapy for the treatment of hematological malignancies
Buchler T.; Michalek J.; Kovarova L.; Musilova R.; Hajek R.
T. Buchler, Dept. of Internal Med.-Hematooncol., Masaryk University Hospital, Jihlavska 20, 639 00 Brno Czech Republic
AUTHOR EMAIL: tbuchler@fnbrno.cz
Hematology (HEMATOLOGY) (United Kingdom) 2003, 8/2 (97-104)
CODEN: HMATF ISSN: 1024-5340
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 86

15/3/11 (Item 11 from file: 73)
DIALOG(R)File 73:EMBASE

12046990 EMBASE No: 2003158588
Prostate cancer: Advances in immunotherapy
Hurwitz A.A.; Yanover P.; Markowitz M.; Allison J.P.; Kwon E.D.
Dr. E.D. Kwon, Depts. of Urology and Immunology, Comprehensive Cancer Center, Mayo Clinic, 200 First Street SW, Rochester, MN 55905 United States
AUTHOR EMAIL: kwon.eugene@mayo.edu
BioDrugs (BIODRUGS) (New Zealand) 2003, 17/2 (131-138)
CODEN: BIDRF ISSN: 1173-8804
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 89

15/3/12 (Item 12 from file: 73)
DIALOG(R)File 73:EMBASE

12045999 EMBASE No: 2003157368
Regional response leading to tumorigenesis after sulindac in small and large intestine of mice with Apc mutations
Yang K.; Fan K.; Kurihara N.; Shinozaki H.; Rigas B.; Augenlicht L.; Kopelovich L.; Edelmann W.; Kucherlapati R.; Lipkin M.
K. Yang, Strang Cancer Research Laboratory, The Rockefeller University, 1230 York Avenue, New York, NY 10021 United States
AUTHOR EMAIL: yangk@mail.rockefeller.edu
Carcinogenesis (CARCINOGENESIS) (United Kingdom) 01 MAR 2003, 24/3 (605-611)
CODEN: CRNGD ISSN: 0143-3334
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 61

15/3/13 (Item 13 from file: 73)
DIALOG(R)File 73:EMBASE

12045138 EMBASE No: 2003156483

Dendritic cells, new tools for vaccination
Colino J.; Snapper C.M.
C.M. Snapper, Department of Pathology, Uniformed Serv. Univ. Hlth. Sci., 4301 Jones Bridge Road, Bethesda, MD 20814 United States
AUTHOR EMAIL: csnapper@usuhs.mil
Microbes and Infection (MICROBES INFECT.) (France) 2003, 5/4 (311-319)
CODEN: MCINF ISSN: 1286-4579
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 31

15/3/14 (Item 14 from file: 73)
DIALOG(R)File 73:EMBASE

12024536 EMBASE No: 2003137507
Follicular dendritic cell tumor in the oro-pharyngeal region: Report of a case and a **review** of the literature
Satoh K.; Hibi G.; Yamamoto Y.; Urano M.; Kuroda M.; Nakamura S.
K. Satoh, Dept. of Oral/Maxillofacial Surgery, School of Medicine, Fujita Health University, Kutsukake-cho, Toyoake-city, Aichi, 470-1192 Japan
AUTHOR EMAIL: kjsato@fujita-hu.ac.jp
Oral Oncology (ORAL ONCOL.) (United Kingdom) 2003, 39/4 (415-419)
CODEN: EJCCE ISSN: 1368-8375
PUBLISHER ITEM IDENTIFIER: S1368837502001380
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 46

15/3/15 (Item 15 from file: 73)
DIALOG(R)File 73:EMBASE

12022837 EMBASE No: 2003134209
Immunology and immunotherapy of colorectal cancer
Dalerba P.; Maccalli C.; Casati C.; Castelli C.; Parmiani G.
Dr. G. Parmiani, U. of Immunotherapy of Human Tumours, Ist. Naz. Stud. e la Cura dei Tumori, Via Venezian 1, 20133 Milan Italy
AUTHOR EMAIL: parmiani@istitutotumori.mi.it
Critical Reviews in Oncology/Hematology (CRIT. REV. ONCOL. HEMATOL.) (Ireland) 01 APR 2003, 46/1 (33-57)
CODEN: CCRHE ISSN: 1040-8428
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 243

15/3/16 (Item 16 from file: 73)
DIALOG(R)File 73:EMBASE

12020768 EMBASE No: 2003131665
Clinical and laboratory evaluation of thrombophilia
Perry S.L.; Ortel T.L.
Dr. T.L. Ortel, Division of Hematology, Duke University Medical Center, Stead Building, Durham, NC 27710 United States
AUTHOR EMAIL: ortel001@mc.duke.edu
Clinics in Chest Medicine (CLIN. CHEST MED.) (United States) 2003, 24/1 (153-170)
CODEN: CCHMD ISSN: 0272-5231
DOCUMENT TYPE: Journal ; Review

LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 150

15/3/17 (Item 17 from file: 73)
DIALOG(R)File 73:EMBASE

12015636 EMBASE No: 2003126563
Tissue engineering the kidney
Hammerman M.R.
Dr. M.R. Hammerman, Renal Division, Department of Medicine, Washington Univ. School of Medicine, 660 S. Euclid Ave., St. Louis, MO 63110 United States
AUTHOR EMAIL: mhammerm@im.wustl.edu
Kidney International (KIDNEY INT.) (United States) 01 APR 2003, 63/4 (1195-1204)
CODEN: KDYIA ISSN: 0085-2538
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 40

15/3/18 (Item 18 from file: 73)
DIALOG(R)File 73:EMBASE

12001396 EMBASE No: 2003112743
Tumor-associated antigens as tools in immunodiagnostics and immunotherapy of breast cancer
EINSATZ TUMORASSOZIIERTER ANTIGENE IN DER IMMUNTHERAPIE UND IMMUNDIAGNOSTIK DES MAMMAKARZINOMS
Guckel B.; Meuer S.; Bastert G.; Wallwiener D.
Dr. B. Guckel, Frauenkl. E.-Karls-Univ. Tubingen, Calwerstrasse 7, 72076 Tubingen Germany
AUTHOR EMAIL: brigitte.gueckel@uni-tuebingen.de
Geburtshilfe und Frauenheilkunde (GEBURTSHILFE FRAUENHEILKD.) (Germany) 01 FEB 2003, 63/2 (130-139)
CODEN: GEFRA ISSN: 0016-5751
DOCUMENT TYPE: Journal ; Review
LANGUAGE: GERMAN SUMMARY LANGUAGE: ENGLISH; GERMAN
NUMBER OF REFERENCES: 70

15/3/19 (Item 19 from file: 73)
DIALOG(R)File 73:EMBASE

11998756 EMBASE No: 2003109712
Cellular immunotherapy after autologous hematopoietic stem cell transplantation: Experimental strategies and clinical experiences
Abken H.; Hombach A.; Reinhard G.; Marten A.; Schlimper C.; Glasmacher A.; Bieber T.; Schmidt-Wolf I.G.H.
I.G.H. Schmidt-Wolf, Medizinische Univ. und Poliklinik 1, Rheinische Friedrich-Wilhelms-Univ., Sigmund-Freud-Street 25, 53105 Bonn Germany
Leukemia and Lymphoma (LEUK. LYMPHOMA) (United Kingdom) 01 APR 2003, 44/4 (583-592)
CODEN: LELYE ISSN: 1042-8194
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 88

15/3/20 (Item 20 from file: 73)

DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11989112 EMBASE No: 2003099666
Role of CD4SUP+ T lymphocytes in antitumor immunity
Rajnavolgyi E.; Lanyi A.
E. Rajnavolgyi, Institute of Immunology, Faculty of Medicine, University of Debrecen, Debrecen H-4012 Hungary
Advances in Cancer Research (ADV. CANCER RES.) (United States) 2003, 87/- (195-245)
CODEN: ACRSA ISSN: 0065-230X
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 236

15/3/21 (Item 21 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11965601 EMBASE No: 2003076877
Immunology of the human genital tract
Johansson M.; Lycke N.Y.
Prof. N.Y. Lycke, Department of Clinical Immunology, University of Goteborg, S-413 46 Goteborg Sweden
AUTHOR EMAIL: nils.lycke@microbio.gu.se
Current Opinion in Infectious Diseases (CURR. OPIN. INFECT. DIS.) (United Kingdom) 2003, 16/1 (43-49)
CODEN: COIDE ISSN: 0951-7375
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

15/3/22 (Item 22 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11936267 EMBASE No: 2003047713
Dendritic cell homeostatis in the regulation of self-reactivity
Ludewig B.; Krebs P.; Junt T.; Bocharov G.
B. Ludewig, Laborforschungsabteilung, Kantonsspital St. Gallen, Haus 09, CH-9007 St. Gallen Switzerland
AUTHOR EMAIL: Burkhard.Ludewig@kssg.ch
Current Pharmaceutical Design (CURR. PHARM. DES.) (Netherlands) 2003, 9/3 (221-231)
CODEN: CPDEF ISSN: 1381-6128
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 141

15/3/23 (Item 23 from file: 73)
DIALOG(R)File 73:EMBASE
(c) 2003 Elsevier Science B.V. All rts. reserv.

11915533 EMBASE No: 2003027102
In vitro generation of IL-10-producing regulatory CD4SUP+ T cells is induced by immunosuppressive drugs and inhibited by Th1- and Th2-inducing cytokines
O'Garra A.; Barrat F.J.
A. O'Garra, Division of Immunoregulation, Natl. Institute for Medical Research, The Ridgeway, Mill Hill, London NW7 1AA United Kingdom
Immunology Letters (IMMUNOL. LETT.) (Netherlands) 22 JAN 2003, 85/2

(135-139)
CODEN: IMLED ISSN: 0165-2478
PUBLISHER ITEM IDENTIFIER: S0165247802002390
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 40

15/3/24 (Item 24 from file: 73)
DIALOG(R)File 73:EMBASE

11911324 EMBASE No: 2003021679
What's new in the treatment of advanced prostate cancer?
Sternberg C.N.
C.N. Sternberg, Department of Medical Oncology, San Camillo-Forlanini Hospital, Vincenzo Pansadoro Foundation, Via Aurelia 559, 00165 Rome Italy
AUTHOR EMAIL: cstern@mclink.it
European Journal of Cancer (EUR. J. CANCER) (United Kingdom) 2003, 39/2 (136-146)
CODEN: EJCAE ISSN: 0959-8049
PUBLISHER ITEM IDENTIFIER: S0959804902006652
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 107

15/3/25 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14899543 22555333 PMID: 12669023
Anatomical basis of tolerance and immunity to intestinal antigens.
Mowat Allan McI
Department of Immunology and Bacteriology, Western Infirmary, Glasgow G11 6NT, UK. a.m.mowat@clinmed.gla.ac.uk
Nature reviews. Immunology (England) Apr **2003**, 3 (4) p331-41, ISSN 1474-1733 Journal Code: 101124169
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

15/3/26 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14751663 22556520 PMID: 12669451
Development of vaccines against self-antigens: the p53 paradigm.
Chada Sunil; Mhashilkar Abner; Roth Jack A; Gabrilovich Dmitry
Introgen Therapeutics Inc, 2250 Holcombe Boulevard, Houston, TX 77030, USA. s.chada@introgen.com
Current opinion in drug discovery & development (England) Mar **2003**, 6 (2) p169-73, ISSN 1367-6733 Journal Code: 100887519
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

15/3/27 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

(c) format only 2003 The Dialog Corp. All rts. reserv.

14751662 22556519 PMID: 12669450
Poxviruses as vectors for cancer immunotherapy.
Kwak Heesun; Horig Heidi; Kaufman Howard L
Columbia University College of Physicians & Surgeons, Departments of Surgery & Pathology, 177 Fort Washington Avenue, MHB-7SK, New York, NY 10032, USA.
Current opinion in drug discovery & development (England) Mar **2003**, 6 (2) p161-8, ISSN 1367-6733 Journal Code: 100887519
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

15/3/28 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

14712477 22505545 PMID: 12618748
Basic and clinical immunology.
Chinen Javier; Shearer William T
Genetics and Molecular Biology Branch, National Human Genome Research Institute, Bethesda, MD, USA.
Journal of allergy and clinical immunology (United States) Mar **2003**, 111 (3 Suppl) pS813-8, ISSN 0091-6749 Journal Code: 1275002
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed

15/3/29 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)
(c) format only 2003 The Dialog Corp. All rts. reserv.

14707860 22544959 PMID: 12658270
Antigen-induced regulatory T cells in autoimmunity.
von Herrath Matthias G; Harrison Leonard C
La Jolla Institute for Allergy and Immunology, Division of Immune Regulation, 10355 Science Center Drive, San Diego, California 92121, USA.
Nature reviews. Immunology (England) Mar **2003**, 3 (3) p223-32, ISSN 1474-1733 Journal Code: 101124169
Document type: Journal Article; Review; Review, Tutorial
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
? ds

Set	Items	Description
S1	192	(DENDRITIC)(20N)(THERAP? OR TREAT?)(30N)(CORRELAT? OR PREDICT?)
S2	96	RD S1 (unique items)
S3	0	S2 AND ATP
S4	459	(ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
S5	81	(ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)(10N)(ADD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
S6	44	RD S5 (unique items)
S7	54	S2 AND (DISEASE? OR IMMUNITY OR VIRAL OR BACTERIAL OR CANCER?)
S8	3	S2 AND REVIEW?
S9	4023	(DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE OR

```
             ADMINIST?)
S10          302   S9 AND REVIEW?
S11          269   RD S10 (unique items)
S12           48   S11 AND PY=2002
S13           48   RD S12 (unique items)
S14           29   S11 AND PY=2003
S15           29   RD S14 (unique items)
? s (dendritic or apc? or antigen(w)present?)(20n)(adoptive or
administ?)(20n)(correlat? or predict?)
Processing
            98249  DENDRITIC
            31425  APC?
          1129519  ANTIGEN
          3815635  PRESENT?
            65658  ANTIGEN(W)PRESENT?
            26246  ADOPTIVE
          3228183  ADMINIST?
          1918476  CORRELAT?
          1055145  PREDICT?
     S16       60  (DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE
                   OR ADMINIST?)(20N)(CORRELAT? OR PREDICT?)
? rd s16
...examined 50 records  (50)
...completed examining records
     S17       33  RD S16 (unique items)
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Set     Items   Description
S1        192   (DENDRITIC)(20N)(THERAP? OR TREAT?)(30N)(CORRELAT? OR PRED-
                ICT?)
S2         96   RD S1 (unique items)
S3          0   S2 AND ATP
S4        459   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)
S5         81   (ATP)(20N)(DENDRITIC OR ANTIGEN(W)PRESENT? OR APC?)(10N)(A-
                DD? OR STIMULAT? OR INCUBAT? OR CULTUR?)
S6         44   RD S5 (unique items)
S7         54   S2 AND (DISEASE? OR IMMUNITY OR VIRAL OR BACTERIAL OR CANC-
                ER?)
S8          3   S2 AND REVIEW?
S9       4023   (DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE OR
                ADMINIST?)
S10       302   S9 AND REVIEW?
S11       269   RD S10 (unique items)
S12        48   S11 AND PY=2002
S13        48   RD S12 (unique items)
S14        29   S11 AND PY=2003
S15        29   RD S14 (unique items)
? s (dendritic or apc? or antigen(w)present?)(20n)(adoptive or
administ?)(20n)(correlat? or predict?)
Processing
          98249  DENDRITIC
          31425  APC?
        1129519  ANTIGEN
        3815635  PRESENT?
          65658  ANTIGEN(W)PRESENT?
          26246  ADOPTIVE
        3228183  ADMINIST?
        1918476  CORRELAT?
        1055145  PREDICT?
     S16      60  (DENDRITIC OR APC? OR ANTIGEN(W)PRESENT?)(20N)(ADOPTIVE
                  OR ADMINIST?)(20N)(CORRELAT? OR PREDICT?)
? rd s16
...examined 50 records  (50)
...completed examining records
     S17      33  RD S16 (unique items)
? t s17/7/all

 17/7/1     (Item 1 from file: 5)
DIALOG(R)File   5:Biosis Previews(R)
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14189708   BIOSIS NO.: 200300183737
Unresponsiveness to lymphoid-mediated signals at the neonatal follicular
  dendritic cell precursor level contributes to delayed germinal center
  induction and limitations of neonatal antibody responses to T-dependent
  antigens.
AUTHOR: Pihlgren Maria(a); Tougne Chantal; Bozzotti Paola; Fulurija Alma;
  Duchosal Michel A; Lambert Paul-Henri; Siegrist Claire-Anne
AUTHOR ADDRESS: (a)Department of Pathology, World Health Organization
  Collaborating Center for Vaccinology and Neonatal Immunology, University
  of Geneva, Centre Medicale Universitaire, Rue Michel Servet 1, 1211,
  Geneva 4, Switzerland**Switzerland E-Mail:
  Maria.Pihlgren@medecine.unige.ch
JOURNAL: Journal of Immunology  170 (6):p2824-2832 March 15 2003 2003
MEDIUM: print
ISSN: 0022-1767
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
```

ABSTRACT: The factors limiting neonatal and infant IgG Ab responses to T-dependent Ags are only partly known. In this study, we assess how these B cell responses are influenced by the postnatal development of the spleen and lymph node microarchitecture. When BALB/c mice were immunized with alum-adsorbed tetanus toxoid at various stages of their immune development, a major functional maturation step for induction of serum IgG, Ab-secreting cells, and germinal center (GC) responses was identified between the second and the third week of life. This **correlated** with the development of the follicular **dendritic** cell (FDC) network, as mature FDC clusters only appeared at 2 wk of age. **Adoptive** transfer of neonatal splenocytes into adult SCID mice rapidly induced B cell follicles and FDC precursor differentiation into mature FDC, indicating effective recruitment and signaling capacity of neonatal B cells. In contrast, adoptive transfer of adult splenocytes into neonatal SCID mice induced primary B cell follicles without any differentiation of mature FDC and failed to correct limitations of tetanus toxoid-induced GC. Thus, unresponsiveness to lymphoid-mediated signals at the level of neonatal FDC precursors delays FDC maturation and GC induction, thus limiting primary Ab-secreting cell responses to T-dependent Ags in early postnatal life.

17/7/2 (Item 2 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

14006393 BIOSIS NO.: 200300000422
Tumor suppression induced by intratumor administration of adenovirus vector expressing NK4, a 4-kringle antagonist of hepatocyte growth factor, and naive dendritic cells.
AUTHOR: Kikuchi Toshiaki(a); Maemondo Makoto; Narumi Koh; Matsumoto Kunio; Nakamura Toshikazu; Nukiwa Toshihiro
AUTHOR ADDRESS: (a)Department of Respiratory Oncology and Molecular Medicine, Institute of Development, Aging and Cancer, Tohoku University, 4-1 Seiryomachi, Aobaku, Sendai, 980-8575, Japan**Japan E-Mail: kikuchi@idac.tohoku.ac.jp
JOURNAL: Blood 100 (12):p3950-3959 December 1 2002 2002
MEDIUM: print
ISSN: 0006-4971
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: NK4, a 4-kringle antagonist of hepatocyte growth factor (HGF), is a potent inhibitor of tumor angiogenesis and functions independently of its HGF-antagonistic activity. We have shown previously that in vivo genetic modification of tumors with an adenovirus vector that expresses NK4 (AdNK4) restrains tumor angiogenesis and slows the rate of tumor growth in vivo. In the present study, we investigated the hypothesis that this can be made more efficient by also **administering** bone marrow-generated **dendritic** cells (DCs) to the tumor. The data show that the growth of mouse subcutaneous tumors is significantly suppressed by direct **administration** of DCs into established tumors that had been pretreated with AdNK4 3 days previously. The synergistic antitumor effect produced by the combination therapy of AdNK4 with DCs **correlated** with the in vivo priming of tumor-specific cytotoxic T lymphocytes. Analysis of mice treated with fluorescence-labeled DCs suggested that DCs injected into the flank tumor could migrate to lymphoid organs in vivo for activation of immune-relevant processes. Knockout mice experiments demonstrated that the tumor regression produced by this combination therapy depends on both major histocompatibility complex (MHC) class I antigen presentation of DCs injected into the tumors and CD8+ T cells of the treated host. Finally, a mechanism for

this synergism was suggested by the histological observation that tumor necrosis and apoptosis were induced by genetic engineering of the tumors to express NK4. These findings should be useful in designing novel strategies that use a combination of 2 monotherapies directed against the vascular and immune systems for cancer therapy.

17/7/3 (Item 3 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13775109 BIOSIS NO.: 200200403930
Preliminary experiences of intralesional immunotherapy in cutaneous metastatic melanoma.
AUTHOR: Ridolfi Laura; Ridolfi Ruggero(a)
AUTHOR ADDRESS: (a)Medical Oncology Department, Pierantoni Hospital, Viale Forlanini 34, I-47100, Forli**Italy E-Mail: dayhonco@ausl.fo.it
JOURNAL: Hepato-Gastroenterology 49 (44):p335-339 March-April, 2002
MEDIUM: print
ISSN: 0172-6390
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background/Aims: **Antigen presenting** cells are inactive within tumor tissue because of local immunosuppression. Tumor infiltrating lymphocyte signal activation transducing mechanisms are also seriously impaired. **Administration** of granulocyte macrophage-colony stimulating factor may lead to **antigen-presenting** cell recovery and interleukin-2 may restore local tumor infiltrating lymphocyte activation. Moreover, interleukin-2 increases the systemic lymphocyte population, an event which seems to **correlate** with a better prognosis. The present phase I-II study was carried out to examine whether intralesional injection of granulocyte macrophage-colony stimulating factor followed by subcutaneous interleukin-2 would induce a clinical response in advanced, pretreated and elderly melanoma patients. Methodology: Fourteen patients over 60 years of age received intralesional granulocyte macrophage-colony stimulating factor (150mug per lesion on day 1), generally divided between the two largest cutaneous lesions, followed by perilesional subcutaneous interleukin-2 (3.000.000/IU) for 5 days (3 to 7) every 3 weeks. All patients received 6 courses of treatment unless progression occurred. Clinical evaluation of the treated cutaneous lesions was assessed at the baseline and before every cycle. Distant lesions were checked every two cycles. Results: Four clinical responses (2 partial responses and 2 minimal responses) (28.5%), which also involved lesions that had not been directly treated, and seven cases of stable disease were observed. The response duration for partial response and minimal response was 9, 4, 4 and 2.5+ months, respectively. Stable disease (50%) recorded in the 7 patients was short term, 3-6 months. Three patients rapidly progressed after 2, 2, and 1 therapy cycles, respectively. The patient who reached the best partial response had a fairly high absolute lymphocyte count (1600 to 2400/mm3). The second one, who reached a complete remission after subsequent locoregional chemotherapy and hyperthermia, had a low absolute lymphocyte count which had doubled, however, by the end of treatment. Blood lymphocyte values in the other patients were too varied to allow any correlation with clinical response. Therapy was well tolerated and only mild fever was observed, with the exception of one patient who had grade 3 fever, with muscle pain and arthralgia. Conclusions: Considering the very low toxicity observed, this treatment might be indicated in elderly patients for whom systemic therapy is no longer a viable option. Improved scheduling and timing could result from further studies.

17/7/4 (Item 4 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13644722 BIOSIS NO.: 200200273543
The role of CTLA-4 in induction and maintenance of peripheral T cell tolerance.
AUTHOR: Eagar Todd N; Karandikar Nitin J; Bluestone Jeffrey A; Miller Stephen D(a)
AUTHOR ADDRESS: (a)Department of Microbiology-Immunology, Northwestern University Medical School, 303 East Chicago Avenue, Chicago, IL, 60611** USA E-Mail: s-d-miller@northwestern.edu
JOURNAL: European Journal of Immunology 32 (4):p972-981 April, 2002
MEDIUM: print
ISSN: 0014-2980
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: T cell receptor engagement and the B7-CD28/CTLA-4 signaling pathways play critical roles in T cell activation and regulation. CD28 engagement results in T cell activation, differentiation and survival while CTLA-4 signals block IL-2 production, cell cycle progression and T cell differentiation. We explored the role of CTLA-4 in peripheral tolerance induced by intravenous **administration** of ethylene carbodiimide-fixed, antigen-coupled splenocytes in the PLP139-151-induced relapsing experimental autoimmune encephalomyelitis system. Tolerance induction with PLP139-151-coupled splenocytes **correlates** with low B7 expression on the fixed **antigen-presenting** cells, conditions that would favor CTLA-4-mediated inhibition. **Administration** of CTLA-4Ig or anti-CTLA-4 concomitant with the 'tolerogenic' stimulus, however, failed to reverse tolerance induction. In contrast, blocking CTLA-4 at the time of secondary 'immunogenic' encounter with antigen reversed the tolerant state. These findings indicate that CTLA-4 is required to maintain the unresponsive state of the tolerized T cells upon antigenic stimulation under inflammatory conditions and, therefore, have important implications for therapeutic regulation of autoimmune disease.

17/7/5 (Item 5 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13104373 BIOSIS NO.: 200100311522
Inhibition of STAT signaling by a JAK-kinase selective inhibitor tyrphostin AG490 enhances antigen-presenting cells (APCs) function in vitro and in vivo.
AUTHOR: Cheng Fengdong(a); Cuenca Alex G(a); Burdelya Luda(a); Huang Mei(a); Jove Richard(a); Yu Hua(a); Sotomayor Eduardo M(a)
AUTHOR ADDRESS: (a)H Lee Moffitt Cancer Center, Tampa, FL**USA
JOURNAL: Blood 96 (11 Part 1):p238a November 16, 2000
MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Bone marrow derived antigen-presenting cells (APCs) play a critical role in priming T-cell responses against tumor antigens. The recent demonstration that APCs are also required for the induction of

T-cell tolerance to tumor antigens places these cells at the center of a critical decision leading to T-cell priming versus tolerance. Although emerging evidence suggest that the maturation/activation status of APCs may influence these highly divergent outcomes, little is known about the mechanism(s)- at the APC level-involved in this critical decision. Macrophages devoid of Signal Transducers and Activators of Transcription-3 (STAT-3) have been shown to be abnormally activated and display increased production of inflammatory cytokines. Therefore, we explored whether inhibition of JAK-STAT signaling by the tyrosine kinase inhibitor tyrphostin AG490, may influence antigen processing and presentation by APCs. In vitro pretreatment of peritoneal macrophages with LPS+AG490 resulted in an enhanced presentation of HA-peptide to naive. CD4+ T cells specific for a MHC class II restricted epitope of influenza hemagglutinin (HA). Indeed, these clonotypic T cells showed enhanced proliferation and IL-2 production as compared to clonotypic T cells that encounter HA-peptide on macrophages pretreated with LPS alone. Furthermore, while LPS-treated macrophages were unable to trigger IFN-g production by clonotypic T cells in response to HA-peptide, macrophages pretreated with LPS+AG490 were able to trigger a fully developed effector function of clonotypic CD4+ T cells, as ascertained by the capacity of these T-cells to produce significant amounts of IFN-g. Importantly, this enhancement of **APCs'** function **correlates** with inhibition of STAT3 DNA-binding activity. In addition, utilizing the **adoptive** transfer system of anti-HA CD4+ T-cells into BALB/c mice, we found that in vivo treatment of these mice with AG490 (0.5 mg/i.p./twice a day x 5 days) enhances the response of antigen-specific T cells to immunization with a recombinant vaccinia encoding HA, suggesting that processing and presentation of antigen by host APC's in vivo could also be enhanced by AG490. These data suggest that blocking JAK-STAT signaling in APCs enhances their antigen-presenting capabilities and raise the intriguing question as to whether this pathway may limit the development of full APC's function needed to effectively prime antigen-specific T-cells.

17/7/6 (Item 6 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11654693 BIOSIS NO.: 199800436424
Antigen expressed on tumor cells fails to elicit an immune response, even in the presence of increased numbers of tumor-specific cytotoxic T lymphocyte precursors.
AUTHOR: Hermans Ian F; Daish Angela; Yang Jianping; Ritchie David S; Ronchese Franca(a)
AUTHOR ADDRESS: (a)Malaghan Inst. Med. Res., P.O. Box 7060, Wellington**New Zealand
JOURNAL: Cancer Research 58 (17):p3909-3917 Sept. 1, 1998
ISSN: 0008-5472
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have used T-cell receptor (TCR) transgenic mice to analyze the interaction of tumors with the immune system. We show that the tumor cell line Lewis lung-lymphocytic choriomeningitis virus (LL-LCMV), genetically manipulated to express an H-2 Db-restricted epitope of the lymphocytic choriomeningitis virus glycoprotein (LCMV33-41), Can grow progressively in TCR transgenic mice, where apprx50% of CD8+ T cells are specific for LCMV33-41. TCR transgenic T cells were not deleted in tumor-bearing mice, and their surface phenotype and cytokine secretion patterns remained typical of naive T cells. Also, TCR transgenic T cells from tumor-bearing mice had undiminished capacity to proliferate to antigen in vitro. Tumor-protective immune responses could be elicited in TCR transgenic mice by immunization with LCMV33-41 peptide-loaded **dendritic** cells.

Tumor resistance **correlated** with the switch of TCR transgenic T cells from a CD44low to a CD44high phenotype and increased capacity to produce IFNgamma in vitro. Results similar to those obtained in TCR transgenic mice were also obtained using an **adoptive** transfer system, where small numbers of TCR transgenic T cells were injected into normal C57BL/6 hosts. These data indicate that even large tumors may not induce specific immunization, tolerance, or anergy to tumor antigens, and that high numbers of tumor-specific CTL precursors are not sufficient to provide tumor resistance.

17/7/7 (Item 7 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

11623078 BIOSIS NO.: 199800405235
Bolus injection of aqueous antigen leads to a high density of T-cell-receptor ligand in the spleen, transient T-cell activation and anergy induction.
AUTHOR: Switzer S K; Wallner B P; Briner T J; Sunshine G H; Bourque C R; Luqman M(a)
AUTHOR ADDRESS: (a)Peptimmune Inc., 840 Memorial Dr., Cambridge, MA 02139** USA
JOURNAL: Immunology 94 (4):p513-522 Aug., 1998
ISSN: 0019-2805
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: In vivo anergy can be modelled by administration of soluble peptide to T-cell receptor (TCR) transgenic mice specific for the moth cytochrome c peptide 88-103 (MCCp). Two weeks after initial peptide treatment, T cells were present in normal numbers but were unresponsive to antigen stimulation in vitro. Only bolus injections of peptide, either subcutaneous or intravenous, were effective at inducing tolerance, while slowly released antigen administered via mini-osmotic pump failed to result in anergy. Examination of T cells soon after bolus peptide administration revealed that anergy induction was preceded by a transient hyperactivation of T cells in vivo. Within 2 hr of peptide treatment, interleukin-2 was detectable in the plasma of the transgenic mice. Interestingly, only bolus injections of peptide led to high levels of T-cell activation, while adjuvant emulsified and pump-administered peptide resulted in very low stimulation in vivo. When the dose of bolus-injected peptide used for tolerization was titrated, the extent of anergy induction directly **correlated** with the intensity of early T-cell activation. Indirect measurements of TCR-ligand density on the surface of **antigen-presenting** cells following peptide **administration** revealed that aqueous peptide delivered via bolus injection generated a large number of major histocompatibility complex-peptide complexes, while pump-delivered and adjuvant-emulsified peptide did not. These data suggest that high levels of TCR ligand are required for in vivo T-cell hyperactivation and induction of anergy.

17/7/8 (Item 8 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

10803172 BIOSIS NO.: 199799424317
The mode of protein antigen administration determines preferential presentation of peptide-class II complexes by lymph node dendritic or B cells.
AUTHOR: Guery Jean-Charles; Ria Francesco; Galbiati Francesca; Smiroldo Simona; Adorini Luciano(a)

AUTHOR ADDRESS: (a)Roche Milano Ricerche, Via Olgettina 58, 20132 Milano** Italy
JOURNAL: International Immunology 9 (1):p9-15 1997
ISSN: 0953-8178
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We have compared the capacity of dendritic cells (DC) and B cells to present peptide-class II complexes following administration of protein in adjuvant or in soluble form. Three different antigen-presenting cell (APC) populations were separated from draining lymph node cells from mice immunized s.c. with hen egg-white lysozyme (HEL) in adjuvant or with adjuvant only followed by soluble HEL: DC (N418+, class II+, B22-, low buoyant density), large B cells (B220+, low buoyant density) and small B cells (B220+, high buoyant density). HEL peptide-class II complexes displayed by these APC were evaluated by their capacity to activate HEL-specific T hybridoma cells. Following immunization with HEL in adjuvant, DC are the only lymph node APC population expressing detectable HEL peptide-class II complexes. Conversely, after i.v. administration of soluble HEL in mice previously injected with adjuvant only, lymph node B cells are much more efficient than DC in presenting peptide-class II complexes to T cells. Therefore, different modes of protein antigen **administration** lead to selective expression of antigenic complexes by different **APC** populations. These data **correlate** with the observation that, unlike B cells, DC recruited in lymph nodes of mice injected with adjuvant only present in vitro processed protein antigen much less efficiently than synthetic peptides, probably as a consequence of their maturation in vivo.

10572476 BIOSIS NO.: 199699193621
Comparison of hemorrhagic effect of heparin and human activated protein C with use of thrombostat 4000.
AUTHOR: Katsuura Yasuhiro(a); Tanabe Hirofumi; Kiyoki Mamoru; Funatsu Akinobu
AUTHOR ADDRESS: (a)Pharm. Dev., Res. Lab., Teijin Ltd., 4-3-2 Ashigoaka, Hino, Tokyo 191**Japan
JOURNAL: Haemostasis 26 (4):p203-209 1996
ISSN: 0301-0147
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The importance of bleeding as a complication of anticoagulant therapy is clearly recognized. We previously reported that amelioration of hemorrhage associated with disseminated intravascular coagulation by the human activated protein C (APC) was greater than that by heparin. In this study, we compared the bleeding complication of intravenously administered APC and heparin in rabbits, and also estimated primary hemostasis. When both anticoagulants were intravenously infused, the bleeding time from a punctured ear vein was prolonged dose-dependently. However, at doses which prolonged the activated partial thromboplastin time nearly equally, the prolongation of bleeding was greater in heparin-**administered** rabbits. Blood withdrawn from heparin-**administered** animals showed increases in in vitro bleeding parameters which **correlated** with the in vivo bleeding time. However, only small changes were observed in the blood withdrawn from **APC-administered** animals. Both drugs induced either no change or only a slight decrease in the platelet count, hematocrit and fibrinogen content. These observations suggest that **APC** may be a

more useful anticoagulant than heparin since it causes less bleeding tendency.

17/7/10 (Item 10 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

09878528 BIOSIS NO.: 199598333446
Pharmacokinetics of human activated protein C: 1st communication: Plasma concentration and excretion of a lyophilized purified human activated protein C after intravenous administration in the mouse and the rabbit.
AUTHOR: Ishii S; Mochizuki T(a); Nagao T; Sugiki S; Kudo S; Harakawa N; Taniguchi K; Igarashi Y; Kondo S; Kiyoki M
AUTHOR ADDRESS: (a)Pharm. Res. Dep., Pharm. Dev. Res. Lab., Inst. Bio-Med. Res., Teijin Ltd., 4-3-2, Asahiga-oka, H**Japan
JOURNAL: Arzneimittel-Forschung 45 (5):p636-644 1995
ISSN: 0004-4172
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English; German

ABSTRACT: Pharmacokinetic studies of human activated protein C (CAS 42617-41-4, APC) were investigated in mice and rabbits with 125I-labeled compound Plasma levels of APC were determined by three different assays: total radioactivity, **APC** antigenicity determined by sandwich enzyme-linked immunosorbent assay (ELISA), and the amidolytic activity which was performed by immunologically captured **APC**. **APC** concentration obtained from these assays were shown to be **correlated** well at early times post-dose. After intravenous **administration**, total radioactivity in the plasma declined tri-exponentially, but antigenicity and amidolytic activity in the plasma declined biexponentially. Plasma AUC increased proportionally with the dose, and the total body clearance and t-1/2 did not change significantly. In addition, no significant difference was observed between the pharmacokinetics in male and female mice. In rabbit study, the profiles of times vs APC concentration in the plasma was similar to those in mice after single bolus injection. The plasma concentrations of APC during and after infusion in rabbits were also determined APC concentration increased during infusion and reached almost steady state at the end of infusion. The profiles of the APC concentration in benzamidine citrate plasma corresponded to the simulated curves which were characterized by the parameters obtained from the single bolus experiment. Plasma disposition profiles of the protein were studied with high performance gel chromatography method. The radioactivity in the unchanged APC was observed at 15 min after administration. At 1 h, most of the radioactivity was observed in larger molecule fraction than the intact APC. These results corresponded to the decrease of amidolytic activity in the plasma. Mass balance studies in mice showed that almost 95% of the administered radioactivity could be accounted for, of which more than 60% were excreted in the urine following an i.v. dose, predominantly as non drug-related radioactivity, even though a small amount of triacetic acid-precipitable radioactivity was excreted via the biliary route.

17/7/11 (Item 11 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07973384 BIOSIS NO.: 000093040962
HEAT-KILLED LISTERIA-MONOCYTOGENES AND LISTERIA-MONOCYTOGENES SOLUBLE ANTIGEN INDUCE CLONABLE CD4-POSITIVE T LYMPHOCYTES WITH PROTECTIVE AND

CHEMOTACTIC ACTIVITIES IN-VIVO
AUTHOR: BROCKE S; HAHN H
AUTHOR ADDRESS: DEP. NEUROLOGY GENETICS, STANFORD UNIVERSITY MED. CENTER, STANFORD, CA 94305-5235, USA.
JOURNAL: INFECT IMMUN 59 (12). 1991. 4531-4539. 1991
FULL JOURNAL NAME: Infection and Immunity
CODEN: INFIB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: In the present study we attempted to analyze the possibility to induce in mice a T-cell response using killed Listeria monocytogenes in adjuvant. Clearly, nonviable antigen is capable of inducing protective and granuloma-forming T cells in C57BL/6-mice when emulsified in complete Freund's adjuvant. These T cells were cloned in vitro by using antigen and irradiated splenocytes as **antigen-presenting** cells, and the clones were characterized in vivo. Listeria-specific T-cell clones showed protective and chemotactic activity upon **adoptive** transfer, although some degree of functional heterogeneity among different clones was observed. The heterogeneous in vivo functions could not be **correlated** with the ability of the clones to produce gamma interferon or T-cell growth factor (interleukin-2 and/or interleukin-4). It was demonstrated that an in vivo relevant fraction of listeria-specific T lymphocytes can be induced by nonviable antigen in complete Freund's adjuvant. These results show that the low immunogenicity of heat-killed bacteria is not due to the expression of specific protective T-cell epitopes only by live bacteria.

17/7/12 (Item 12 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07906146 BIOSIS NO.: 000093005269
CHLOROQUINE ATTENUATES HEMORRHAGIC SHOCK-INDUCED SUPPRESSION OF KUPFFER CELL ANTIGEN PRESENTATION AND MAJOR HISTOCOMPATIBILITY COMPLEX CLASS II ANTIGEN EXPRESSION THROUGH BLOCKADE OF TUMOR NECROSIS FACTOR AND PROSTAGLANDIN RELEASE
AUTHOR: ERTEL W; MORRISON M H; AYALA A; CHAUDRY I H
AUTHOR ADDRESS: SHOCK TRAUMA RES. LAB., DEP. SURGERY, B424 CLINICAL CENT., MICH. STATE UNIV., EAST LANSING, MICH. 48824.
JOURNAL: BLOOD 78 (7). 1991. 1781-1788. 1991
FULL JOURNAL NAME: Blood
CODEN: BLOOA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Hemorrhagic shock suppresses the ability to Kupffer cells (KC) to present antigen and express the major histocompatibility complex class II (Ia) antigen. These alterations are concomitant with an enhanced release of cytokines (tumor necrosis factor [TNF], interleukin-1 [IL-6], IL-6) and prostaglandin E2 (PGE2) by KC after hemorrhagic shock. The aim of this study was to determine whether chloroquine (CQ) administration in vivo before or after hemorrhage affects the altered cytokine and PGE2 release by KC as well as the capacity of KC to present antigen and express Ia. To study this, C3H/HeN mice were bled to and maintained at a mean arterial blood pressure of 35 mm Hg for 60 minutes, followed by fluid resuscitation. Chloroquine (10 mg/kg body weight) was injected intramuscularly 2 hours before or during resuscitation following shock. The administration of CQ led to a significant reduction in the hemorrhage-induced elevation of TNF, IL-6, and PGE2 release by KC; however, IL-1 secretion was not affected by CQ. In addition, CQ treatment abolished the hemorrhage-induced increase in circulating TNF and IL-6. These changes in cytokines and PGE2 release following CQ

administration correlated with a significant enhancement of the **antigen-presenting** capacity of KC. No differences were observed between pretreatment and posttreatment with CQ. Our data indicate that CQ selectively inhibits the release of TNF, IL-6, and PGE2 by KC, while IL-1 secretion was unaffected. Because the reduction of these inflammatory mediators was concomitant with a significant improvement of KC capacity to present antigen and express Ia, we propose that TNF, IL-6, and PGE2 play a pivotal role in the induction of posthemorrhage immunosuppression. Furthermore, the data suggest that the suppression of KC functions occurs during or after resuscitation, because posttreatment with CQ was as effective as pretreatment. Additional studies indicated that the survival of animals after hemorrhage and sepsis was significantly increased by posttreatment of hemorrhaged mice with CQ. Thus, CQ, because of its unique ability to selectively inhibit the release of inflammatory cytokines and prostaglandins, represents a potent immunomodulating agent in the treatment of conditions associated with increased cytokine release and for decreasing the mortality from sepsis after hemorrhage.

17/7/13 (Item 13 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

07019063 BIOSIS NO.: 000089110947
ROLE OF PROTEIN C IN ENDOTOXIN-INDUCED RELEASE OF PLASMINOGEN ACTIVATOR INHIBITOR FROM ENDOTHELIAL CELL
AUTHOR: OKAJIMA K; KOGA S; NAKAGAKI T; OKABE H; FUNATSU A; TAKATSUKI K
AUTHOR ADDRESS: DEP. LAB. MED., KUMAMOTO UNIV. MED. SCH., KUMAMOTO, JAPAN.
JOURNAL: ACTA HAEMATOL JPN 52 (7). 1989. 1159-1164. 1989
FULL JOURNAL NAME: Acta Haematologica Japonica
CODEN: NKGZA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: To elucidate the role of protein C (PC) in the release of plasminogen activator inhibitor (PAI) from endothelial cells, the effect of PC and activated protein C (APC) on plasma levels of PAI in endotoxin (ET)-treated rats was examined. When activated by snake venom, human PC significantly prolonged the activated partial thromboplastin time (APTT) of both human and rat plasma samples. Addition of APC also prolonged the APTT of both human and rat plasma samples. PAI activity in plasma from septicemic patients and ET-treated rats was neutralized by **APC**. A small dose of ET (0.1 .mu.g/kg) gradually increased plasma PAI activity, which became maximum 3h after ET-treatment. **APC administered** either before or after ET-treatment significantly decreased PAI activity in plasma. When **administered** prior to ET-treatment, PC decreased PAI activity, however, no such inhibition was seen when **administered** after ET-treatment. A significant negative **correlation** between PC concentrations and PAI activities was observed in plasma from septicemic patients. These findings indicated that activation of PC on endothelial surface plays a regulatory role in releasing PAI and that endotoxin might inhibit the surface activation of PC.

17/7/14 (Item 14 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

06779048 BIOSIS NO.: 000088088485
EXPERIMENTAL STUDY ON LANGERHANS CELL DENSITY OF GUINEA-PIG TREATED WITH STEROID AND NON-STEROID IMMUNOSUPPRESSANTS
AUTHOR: CHOI M S; HONG C K; RO B I; CHO S S; CHANG C Y

AUTHOR ADDRESS: DEP. DERMATOL., COLL. MED., CHUNG-ANG UNIVERSITY, SEOUL 156-756, KOREA.
JOURNAL: CHUNG-ANG J MED 14 (2). 1989. 227-242. 1989
FULL JOURNAL NAME: Chung-Ang Journal of Medicine
CODEN: CJMED
RECORD TYPE: Abstract
LANGUAGE: KOREAN

ABSTRACT: Langerhans cells (LC) are known to be immune macrophages of the epidermis and to play a crucial role as antigen presenting cells in the induction of positive immune responses to antigens presented through the skin. Because of their location in the epidermis, they are subject to many environmental toxins as well as epicutaneous medications. This study was undertaken to investigate the influence of topical and systemic administration of immunosuppressants on both Langerhans cells and their antigen presenting capacity in the Guinea pig. Hydrocortisone, prednisolone, cyclosporine A and azathioprine were administrated daily for 10 consecutive days by either topical application to skin, intraperitoneal injection or oral administration. LC densities were determined on the day following cessation of treatment by staining for the plasma membrane-bound ATPase in the EDTA-treated epidermal sheet preparation. DNFB-induced hypersensitivities were assayed by measuring the increment of ear swelling. All immunosuppressants caused a significant reduction in ATPase-positive LC of the epidermis. Both topical application and systemic administration of immunosuppressants depleted the skin of LC, although topical treatment proved to be in a greater decrease in LC density than systemic **administration**. Furthermore, the decrease obtained in LC density **correlated** with substantial impairment in inducing hypersensitivity of the skin. The above finding suggested that immunosuppressants exert their inhibitory effect on contact hypersensitivity through suppression LC density and **antigen-presenting** function of these cells.

17/7/15 (Item 15 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

05645361 BIOSIS NO.: 000083118508
EFFECT OF ORALLY ADMINISTERED AROMATIC RETINOID ON MURINE LANGERHANS CELLS
AUTHOR: SHIOHARA T; KOBAYASHI M; NARIMATSU H; NAGASHIMA M
AUTHOR ADDRESS: DEP. DERMATOL., KYORIN UNIV. SCH. MED., 6-20-2 SHINKAWA, MITAKA, TOKYO 181, JPN.
JOURNAL: ARCH DERMATOL RES 279 (3). 1987. 198-203. 1987
FULL JOURNAL NAME: Archives of Dermatological Research
CODEN: ADRED
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effect of orally administered aromatic retinoid (Ro 10-9359) on murine epidermal Langerhans cells (LC) was studied in vivo and in vitro. Daily administration of retinoid caused a transient increase in Lc density, as determined by staining for Ia antigens, during the first few days of treatment and thereafter a continuing decrease that reached a maximum at 2 weeks. In addition, the morphology and location in the epidermis had been altered. When the treatment was continued to 4 weeks, the density of LC returned to normal. The Ia-**antigen-presenting** function of epidermial cells to an allo-Ia-reactive cloned T cell line was elevated at all stages of retinoid treatment examined. This elevation did not **correlate** with the density of histochemically stainable Ia+ LC. These findings suggest that orally **administered** retinoid profoundly alters the functional capacity of Ia+ LC.

17/7/16 (Item 16 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

03611421 BIOSIS NO.: 000074026998
EFFECT OF GLUCO CORTICO STEROIDS ON EPIDERMAL LANGERHANS CELLS
AUTHOR: BELSITO D V; FLOTTE T J; LIM H W; BAER R L; THORBECKE G J; GIGLI I
AUTHOR ADDRESS: DEP. DERMATOL., N.Y. UNIV. MED. CENT., 550 FIRST AVE., NEW YORK 10016.
JOURNAL: J EXP MED 155 (1). 1982. 291-302. 1982
FULL JOURNAL NAME: Journal of Experimental Medicine
CODEN: JEMEA
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: The effects of topical and systemic administration of various glucocorticoids on the density of epidermal Langerhans cells (LC) were studied in guinea pigs. Glucocorticoids, such as betamethasone dipropionate and valerate, caused a marked decrease in LC demonstrable by staining for cell membrane ATPase activity and Ia antigens. By EM, LC also showed morphologic alterations. The observed decrements in LC density **correlated** with the concentration and known vasoconstrictive potency of the glucocorticoids **administered**. The antiinflammatory action of glucocorticoids in skin disorders may be through their ability to alter epidermal LC, thus interfering with the **antigen-presenting** functions of these cells.

17/7/17 (Item 17 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02661181 BIOSIS NO.: 000067049247
EXPERIMENTAL AND HISTOCHEMICAL STUDIES OF THE HIPPOCAMPAL FORMATION
AUTHOR: OKANO H
AUTHOR ADDRESS: DEP. ANAT., OKAYAMA UNIV. MED. SCH., OKAYAMA, JPN.
JOURNAL: OKAYAMA IGAKKAI ZASSHI 90 (3-4). 1978. 461-478. 1978
FULL JOURNAL NAME: Okayama Igakkai Zasshi
CODEN: OIZAA
RECORD TYPE: Abstract
LANGUAGE: JAPANESE

ABSTRACT: The hippocampal formation of rat brain was studied by the silver sulfide method and was also observed by EM after the administration of dithizone, alloxan and oxine, respectively. In the normal rat, the reaction products were found in the mossy fibers of granular cells of gyrus dentatus which ended at the dendrites of pyramydal cells present in the h3, h4 and h5 areas of the hippocampus. By EM observation, the mossy fiber endings of normal brain were filled with synaptic vesicles, and most of them ended at the **dendritic** spines of pyramidal cells. Zn, shown by the silver sulfide method, was not detected in the hippocampal formation from 1-3 h after the **administration** of dithizone. Simultaneously the number of synaptic vesicles of the mossy fiber endings was decreased and the **dendritic** spines became smooth. Alloxan had no effect on the amount of Zn and the number of synaptic vesicles in mossy fibers, but both decreased temporarily 5-15 min after **administration** of oxine. The **correlation** between Zn and synaptic vesicles in mossy fibers, and the mechanism of these drugs' action to Zn content and synaptic vesicles were discussed.

17/7/18 (Item 18 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

02459235 BIOSIS NO.: 000066041779
EVOKED AND SPONTANEOUS CORTICOFUGAL MULTIPLE UNIT ACTIVITY DURING DIFFERENT PHASES OF METRAZOLE INFUSION IN CATS
AUTHOR: JOY R M; WONG D L
AUTHOR ADDRESS: DEP. PHYSIOL. SCI., SCH. VET. MED., UNIV. CALIF., DAVIS, CALIF. 95616, USA.
JOURNAL: NEUROPHARMACOLOGY 17 (4-5). 1978 281-294. 1978
FULL JOURNAL NAME: Neuropharmacology
CODEN: NEPHB
RECORD TYPE: Abstract
LANGUAGE: ENGLISH

ABSTRACT: Multiple unit activity (MUA) was recorded from the cerebral peduncle during preictal, ictal and postictal phases of Metrazol infusion in cats. During preictal EEG paroxysmal activity MUA activity increased, sustained MUA discharge preceded the onset of tonic EEG seizure activity and bursts of MUA activity coincided with positive transients during late tonic and clonic periods. No MUA discharge was observed during postictal depression. During preictal periods, Metrazol increased the amplitude and duration of the initial MUA burst to stimulation of the ventralis posterolateralis nucleus. The duration and intensity of the MUA suppression following the response was increased. The burst-suppression pattern of MUA activity during repetitive stimulation was replaced by a burst-sustained discharge pattern. The changes observed in EEG and MUA are **correlated** with previously described intracellular changes and provide a consistent picture of EEG, neuronal and axonal behavior during Metrazol **administration**. Axonal activity provides a more relevant indication of effective corticofugal activity than does intracellular recording. The level of axonal discharge **correlates** better with the degree of soma-**dendritic** depolarization than it does to somatic spike generation.

17/7/19 (Item 1 from file: 73)
DIALOG(R)File 73:EMBASE

11836463 EMBASE No: 2002408867
What's the matter with HIV-directed killer T cells?
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AUTHOR EMAIL: wick@scharp.org
Journal of Theoretical Biology (J. THEOR. BIOL.) (United Kingdom) 2002, 219/1 (19-31)
CODEN: JTBIA ISSN: 0022-5193
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 74

That HIV-specific cytotoxic T-lymphocytes (CTLs) might be defective in some way has stimulated much controversy and research. We use mathematical models to explore the predictions of two competing CTL-defect theories: "defective memory" and "defective activation". We discuss whether these models are consistent with adoptive-transfer experiments in HIV-infected patients and vaccine trials in simian immunodeficiency virus (SIV)-infected monkeys. Finally, we describe experimental tests that could decide among these two theories and a competitor: CTL exhaustion.

17/7/20 (Item 2 from file: 73)
DIALOG(R)File 73:EMBASE

11777809 EMBASE No: 2002351139
Real-time monitoring of immune responses
Wieder E.D.
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Cytotherapy (CYTOTHERAPY) (United Kingdom) 2002, 4/4 (347-352)
CODEN: CYTRF ISSN: 1465-3249
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 39

With the advent of cellular immunotherapy, the ability to monitor immune responses during treatment will be essential to evaluate the effectiveness of the new therapies. While the ultimate determinate of the success of immunotherapy trials will be clinical outcome, methods of monitoring immunity in real-time have become available that will assist in the development of immunotherapy strategies and in the prediction of individual patient prognosis during the course of treatment. The essentials of existing immune assays are described here with examples of how these techniques have been used previously. A perspective on which approaches will likely prove the most useful for monitoring immune responses in real-time during immunotherapy is also presented.

17/7/21 (Item 3 from file: 73)
DIALOG(R)File 73:EMBASE

11608192 EMBASE No: 2002179688
Immature mouse dendritic cells enter inflamed tissue, a process that requires E- and P-selectin, but not P-selectin glycoprotein ligand 1
Pendl G.G.; Robert C.; Steinert M.; Thanos R.; Eytner R.; Borges E.; Wild M.K.; Lowe J.B.; Fuhlbrigge R.C.; Kupper T.S.; Vestweber D.; Grabbe S.
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Blood (BLOOD) (United States) 01 FEB 2002, 99/3 (946-956)
CODEN: BLOOA ISSN: 0006-4971
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 49

Inflammatory processes are associated with the rapid migration of dendritic cells (DCs) to regional lymph nodes and depletion of these potent antigen-presenting cells (APCs) from the inflamed tissue. This study examined whether sites of cutaneous inflammation can be repopulated with DCs from a pool of immature DCs circulating in the blood. In adoptive transfer experiments with ex vivo-generated radioactively labeled primary bone marrow-derived DCs injected into mice challenged by an allergic contact dermatitis reaction, immature DCs were actively recruited from the blood to sites of cutaneous inflammation, whereas mature DCs were not. Immature, but not mature, DCs were able to adhere specifically to immobilized recombinant E- and P-selectin under static as well as under flow conditions. P-selectin-dependent adhesion of immature DCs correlates with their higher level of expression of the carbohydrate epitope cutaneous lymphocyte-associated antigen (CLA) and is blocked by a novel inhibitory antibody against mouse P-selectin glycoprotein ligand 1 (PSGL-1). Surprisingly, however, emigration of immature DCs into inflamed skin is retained in the presence of this anti-PSGL-1 antibody and is also normal

when immature DCs are generated from fucosyltransferase (Fuc-T) Fuc-TVII-deficient mice. By contrast, emigration of wild-type immature DCs is reduced by adhesion-blocking anti-E- and P-selectin antibodies, and immature DCs generated ex vivo from Fuc-TVII/Fuc-TIV double-deficient mice emigrate poorly. Thus, fucosylated ligands of the endothelial selectins, determined in part by Fuc-TIV, and independent of PSGL-1, are required for extravasation of DCs into sites of cutaneous inflammation. (c) 2002 by The American Society of Hematology.

17/7/22 (Item 4 from file: 73)
DIALOG(R)File 73:EMBASE

11511944 EMBASE No: 2002085729
Clinical cancer vaccine trials
Jager E.; Jager D.; Knuth A.
E. Jager, II. Medizinische Klinik, Hamatologie - Onkologie, Steinbacher Hohl 2-26, 60488 Frankfurt Germany
AUTHOR EMAIL: EJ200161@aol.com
Current Opinion in Immunology (CURR. OPIN. IMMUNOL.) (United Kingdom) 01 APR 2002, 14/2 (178-182)
CODEN: COPIE ISSN: 0952-7915
DOCUMENT TYPE: Journal ; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 42

Antigens that are selectively or abundantly expressed in cancer cells have been used for clinical trials, mostly in patients with advanced disease, and appear to be better vaccines than whole cells. Candidate vaccines have emerged from different categories of cancer antigens. Strategies involving various forms of peptides have been used either alone or combined with different cytokines, adjuvants or **dendritic** cells to enhance specific immune responses. Although individual patients have benefited, no strategy has emerged as universally applicable; neither has any route of **administration**. Increasingly sensitive methods have **correlated** clinical responses with measurable immune responses to vaccination in some patients.

17/7/23 (Item 5 from file: 73)
DIALOG(R)File 73:EMBASE

11324559 EMBASE No: 2001339737
Intralesional granulocyte-monocyte colony-stimulating factor followed by subcutaneous interleukin-2 in metastatic melanoma: A pilot study in elderly patients
Ridolfi L.; Ridolfi R.; Ascari-Raccagni A.; Casadei S.; Gatti A.; Trevisan G.; Righini M.G.
L. Ridolfi, Department of Medical Oncology, Morgagni-Pierantoni Hospital, Viale Forlanini 34, I-47100 Forli Italy
AUTHOR EMAIL: dayhonco@ausl.fo.it
Journal of the European Academy of Dermatology and Venereology (J. EUR. ACAD. DERMATOL. VENEREOL.) (United Kingdom) 2001, 15/3 (218-223)
CODEN: JEAVE ISSN: 0926-9959
DOCUMENT TYPE: Journal ; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 33

Aim and background. Recent data in the literature indicate that antigen-presenting cells (APC) are inactive in tumour tissue because of local immunosuppression. Tumour-infiltrating lymphocyte (TIL) signal activation transducing mechanisms are also seriously impaired.

Administration of granulocyte macrophage-colony stimulating factor (GM-CSF) may lead to **APC** recovery and interleukin (IL)-2 may restore local TIL activation. Moreover, IL-2 increases the systemic lymphocyte population, an event that seems to **correlate** with a better prognosis. Study design. The present phase I-II study was carried out to examine whether intralesional injection of GM-CSF followed by subcutaneous IL-2 would induce a clinical response in advanced, pretreated elderly melanoma patients. Methods. Sixteen patients over 60 years of age received intralesional GM-CSF (150 ng per lesion on day 1), generally divided between the two largest cutaneous lesions, followed by perilesional subcutaneous IL-2 (3 000 000 IU) for 5 days (days 3-7 inclusive) every 3 weeks. Results. Four clinical responses [two partial (PR) and two minimal (MR)] (25%), which also involved lesions that had not been directly treated, and nine cases of stable disease were observed. The response duration for PR and MR was 9, 4, 4 and 2.5+ months, respectively. Stable disease (56%) recorded in the nine patients was short-term (3-6 months). Three patients rapidly progressed after two, two and one therapy cycles, respectively. The patient who reached the best PR had a fairly high absolute lymphocyte count (1600-2400/mmSUP3). The second one, who reached complete remission after subsequent locoregional chemotherapy and hyperthermia, however, had a low absolute lymphocyte count that had doubled by the end of treatment. Blood lymphocyte values in the other patients were too varied to allow any correlation with clinical response. Therapy was well tolerated and only mild fever was observed, with the exception of one patient who had grade 3 fever, with muscle pain and arthralgia. Conclusions. Considering the very low toxicity observed, this treatment might be indicated in elderly patients for whom systemic therapy is no longer a viable option. Improved scheduling and timing could result from further studies.

17/7/24 (Item 6 from file: 73)
DIALOG(R)File 73:EMBASE

11222649 EMBASE No: 2001237518
Immunological and molecular analysis of the sentinel lymph node: A potential approach to predict outcome, tailor therapy, and optimize parameters for tumor vaccine development
Meijer S.L.; Dols A.; Hu H.-M.; Jensen S.; Poehlein C.H.; Chu Y.; Winter H.; Yamada J.; Moudgil T.; Wood W.J.; Doran T.; Justice L.; Fisher B.; Wisner R.; Wood J.; Vetto J.T.; Mehrotra R.; Rosenheim S.; Weinberg A.D.; Bright R.; Walker E.; Puri R.; Smith II J.W.; Urba W.J.; Fox B.A.
B.A. Fox, Robert W. Franz Can. Research Center, Earle A. Chiles Research Institute, 4805 N.E. Glisan, Portland, OR 97213-2967 United States
Journal of Clinical Pharmacology (J. CLIN. PHARMACOL.) (United States) 2001, 41/7 SUPPL. (81S-94S)
CODEN: JCPCB ISSN: 0091-2700
DOCUMENT TYPE: Journal ; Conference Paper
LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 97

17/7/25 (Item 7 from file: 73)
DIALOG(R)File 73:EMBASE

10732314 EMBASE No: 2000141864
Beneficial effects of postmenopausal hormone replacement therapy with transdermal estradiol on sensitivity to activated protein C
De Mitrio V.; Marino R.; Cicinelli E.; Galantino P.; Di Bari L.; Giannoccaro F.; De Pergola G.; Lapecorella M.; Schonauer S.; Schiraldi O.
Prof. V. De Mitrio, Via Tanzi 43, 70121 Bari Italy
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Blood Coagulation and Fibrinolysis (BLOOD COAGUL. FIBRINOLYSIS) (United Kingdom) 2000, 11/2 (175-182)
CODEN: BLFIE ISSN: 0957-5235
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH
NUMBER OF REFERENCES: 35

Many hemostatic and fibrinolytic parameters have been evaluated following hormone replacement therapy (HRT) but little is known about its influence on the anticoagulant response to activated protein C (APC- sensitivity). For this purpose, we studied the effect of transdermal 17-beta- estradiol (50 mug/24 h) by a continuous regimen on the APC-sensitivity, in 28 postmenopausal hysterectomized women (mean age, 47 years; range, 44-65 years). We also measured the plasma proteins directly involved in the protein C anticoagulant pathway, such as activities of factor VIII (VIII:C), factor V and free protein S. Von Willebrand factor (vWF) antigen, the carrier protein of factor VIII, was also determined. Blood sampling was done at baseline and after 16-week therapy. A significant increase in the normalized APC- sensitivity ratio (n-APC-SR) values (mean +/- SD: pre-trial, 0.88 +/- 0.14; post-trial, 1.01 +/- 0.12; P < 0.001) and a significant decrease of factor VIII:C plasma levels (pre-trial, 1.13 +/- 0.29 IU/ml; post-trial, 0.98 +/- 0.20 IU/ml; P=0.001) were found. No difference was observed in factor V, protein S and vWF plasma levels. **Correlation** studies demonstrated only a significant negative **correlation** between the percent change in n-**APC**-SR and the percent change in factor VIII:C (r = -0.574; P = 0.001). Our findings clearly show that HRT with transdermal estradiol improves the anticoagulant response to **APC**, probably as a result of a decreased factor VIII:C. We also suggest that a similar but opposite mechanism may occur for perorally **administered** estrogens used in the HRT. These results may have some clinical implications about the reported increase of the risk for venous thromboembolism following HRT. (C) 2000 Lippincott Williams and Wilkins.

17/7/26 (Item 8 from file: 73)
DIALOG(R)File 73:EMBASE

06402146 EMBASE No: 1996060273
The failure of current immunotherapy for malignant glioma. Tumor-derived TGF-beta, T-cell apoptosis, and the immune privilege of the brain
Weller M.; Fontana A.
Neurologische Klinik, Universitat Tubingen, Hoppe-Seyler-Strasse 3,72076 Tubingen Germany
Brain Research Reviews (BRAIN RES. REV.) (Netherlands) 1995, 21/2 (128-151)
CODEN: BRERD ISSN: 0165-0173
DOCUMENT TYPE: Journal; Review
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

Human malignant gliomas are rather resistant to all current therapeutic approaches including surgery, radiotherapy and chemotherapy as well as antibody-guided or cellular immunotherapy. The immunotherapy of malignant glioma has attracted interest because of the immunosuppressed state of malignant glioma patients which resides mainly in the T-cell compartment. This T-cell suppression has been attributed to the release by the glioma cells of immunosuppressive factors like transforming growth factor-beta (TGF-beta) and prostaglandins. TGF-beta has multiple effects in the immune system, most of which are inhibitory. TGF-beta appears to control downstream elements of various cellular activation cascades and regulates the expression of genes that are essential for cell cycle progression and mitosis. Since TGF-beta-mediated growth arrest of T-cell lines results in their apoptosis in vitro, glioma-derived TGF-beta may prevent

immune-mediated glioma cell elimination by inducing apoptosis of tumor-infiltrating lymphocytes in vivo. T-cell apoptosis in the brain may be augmented by the absence of professional **antigen-presenting** cells and of appropriate costimulating signals. Numerous in vitro studies **predict** that tumor-derived TGF-beta will incapacitate in vitro-expanded and locally **administered** lymphokine-activated killer cells (LAK-cells) or tumor-infiltrating lymphocytes. Thus, TGF-beta may be partly responsible for the failure of current adoptive cellular immunotherapy of malignant glioma. Recent experimental in vivo studies on non-glial tumors have corroborated that neutralization of tumor-derived TGF-beta activity may facilitate immune-mediated tumor rejection. Current efforts to improve the efficacy of immunotherapy for malignant glioma include various strategies to enhance the immunogenicity of glioma cells and the cytotoxic activity of immune effector cells, e.g., by cytokine gene transfer. Future strategies of cellular immunotherapy for malignant glioma will have to focus on rendering glioma cell-targeting immune cells resistent to local inactivation and apoptosis which may be induced by TGF-beta and other immunosuppressive molecules at the site of neoplastic growth. Cytotoxic effecters targeting Fas/APO-1, the receptor protein for perforin-independent cytotoxic T-cell killing, might be promising, since Fas/APO-1 is expressed by glioma cells but not by untransformed brain cells, and since Fas/APO-1-mediated killing in vitro is not inhibited by TGF-beta.

17/7/27 (Item 9 from file: 73)
DIALOG(R)File 73:EMBASE

04875342 EMBASE No: 1992015557
Heat-killed Listeria monocytogenes and L. monocytogenes soluble antigen induce clonable CD4sup + T lymphocytes with protective and chemotactic activities in vivo
Brocke S.; Hahn H.
Department of Neurology, Stanford University, Medical Center,Stanford, CA 94305-5235 United States
Infection and Immunity (INFECT. IMMUN.) (United States) 1991, 59/12 (4531-4539)
CODEN: INFIB ISSN: 0019-9567
DOCUMENT TYPE: Journal; Article
LANGUAGE: ENGLISH SUMMARY LANGUAGE: ENGLISH

In the present study we attempted to analyze the possibility to induce in mice a T-cell response using killed Listeria monocytogenes in adjuvant. Clearly, nonviable antigen is capable of inducing protective and granuloma-forming T cells in C57BL/6 mice when emulsified in complete Freund's adjuvant. These T cells were cloned in vitro by using antigen and irradiated splenocytes as **antigen-presenting** cells, and the clones were characterized in vivo. Listeria-specific T-cell clones showed protective and chemotactic activity upon **adoptive** transfer, although some degree of functional heterogeneity among different clones was observed. The heterogeneous in vivo functions could not be **correlated** with the ability of the clones to produce gamma interferon or T-cell growth factor (interleukin-2 and/or interleukin- 4). It was demonstrated that an in vivo relevant fraction of listeria- specific T lymphocytes can be induced by nonviable antigen in complete Freund's adjuvant. These results show that the low immunogenicity of heat- killed bacteria is not due to the expression of specific protective T-cell epitopes only by live bacteria.

17/7/28 (Item 10 from file: 73)
DIALOG(R)File 73:EMBASE

01571501 EMBASE No: 1980191913
On the origin and mode of action of functionally distinct macrophage subpopulations
Lee K.C.
Dept. Immunol., Med. Sci. Bldg, Univ. Alberta, Edmonton, T6G 2H7 Canada
Molecular and Cellular Biochemistry (MOL. CELL. BIOCHEM.) (Netherlands)
1980, 30/1 (39-55)
CODEN: MCBIB
DOCUMENT TYPE: Journal
LANGUAGE: ENGLISH

Functionally distinct subpopulations of macrophages at various stages of differentiation can be separated by fractionation of murine peritoneal cells according to size, since the maturation of monocytes into macrophages is associated with cell enlargement. For immunostimulatory functions which can be served by macrophage-derived factors, normal macrophages of all sizes will function very well. However, in the antigen-specific T cell proliferative response which requires the presentation of antigen on the surface of macrophages bearing determinants (Ia) specified by the I-region of the major histocompatibility complex, only small, and hence relatively immature, macrophages will stimulate. This **antigen-presenting** activity is **predictably** sensitive to treatment with antisera specific for Ia. Intraperitoneal **administration** of the adjuvant, Corynebacterium parvum, induces the appearance of cytostatic and cytolytic activity against tumor cells. This activity is associated with the largest macrophages which are separable from the small, immunostimulatory macrophages. Thus the maturation of monocytes can be envisaged as following a linear sequence from the Iasup + antigen-presenting cells to the cytocidal activated macrophages. An alternative approach to the problem of macrophage heterogeneity is the cultivation of macrophages from bone marrow precursors in vitro. Antigen-presenting activity develops during the exponential phase of growth to varying degrees depending on the source of the colony stimulating factors used in the bone marrow cultures and on the antigen used for immune stimulation. Although culture-grown macrophages are as active as normal splenic or peritoneal macrophages at presenting large antigens, they are clearly deficient at presenting small antigens. Cell size fractionation of exponentially growing bone marrow cultures has revealed that the antigen-presenting cells are small macrophages, but their position in the cell cycle and their developmental relationship to macrophages in vivo have not been elucidated.

17/7/29 (Item 1 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

14945015 22678883 PMID: 12794428
Activation of protein C following infusion of protein C concentrate in children with severe meningococcal sepsis and purpura fulminans: A randomized, double-blinded, placebo-controlled, dose-finding study.
De Kleijn Ester D; De Groot Ronald; Hack C Erik; H Mulder Paul G; Engl Werner; Moritz Berta; Joosten Koen F M; Hazelzet Jan A
Critical care medicine (United States) Jun 2003, 31 (6) p1839-47, ISSN 0090-3493 Journal Code: 0355501
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: In Process
BACKGROUNDMeningococcal septic shock in children results in high mortality and morbidity, and decreased protein C levels in these patients are associated with a poor outcome. We carried out a randomized, double-blinded, placebo-controlled study by supplying protein C concentrate. This phase 2 study was designed to assess the activation process of protein C and to study the dosing regimen of protein C

concentrate in children with purpura fulminans and meningococcal septic shock in the perspective of a possible phase 3 trial.METHODSForty children were randomized to receive placebo or protein C concentrate (200 IU/kg, 400 IU/kg, or 600 IU/kg), for a maximum of 7 days. Clinical and laboratory data, including plasma levels of protein C and activated protein C (APC), were collected at various time points. All patients received standard therapy for septic shock, including antibiotics, inotropic/vasoactive drugs, and blood products.RESULTSIncreased **APC** levels relative to baseline were observed for the 27 of 28 patients treated with protein C concentrate, and the areas under the curve of protein C and **APC** were **correlated** with the dosage of protein C concentrate **administered** . Activation of coagulation, as evidenced by d-dimer levels, as well as the ratio of thrombin vs. **APC** normalized significantly faster with increasing dosages of protein C concentrate. No adverse reactions related to protein C concentrate were observed. Nine of the 40 (23%) patients died, and five survivors required amputations, with no differences in these rates among the randomized groups. Baseline APC levels were positively correlated with sequential organ failure assessment and pediatric risk of mortality scores and with d-dimers, tumor necrosis factor-alpha, interleukin-1, interleukin-6, interleukin-8, plasminogen activator inhibitor-1, TAT complexes, and PAP complexes.CONCLUSIONSTreatmen t with protein C concentrate is safe in children with purpura fulminans and meningococcal septic shock and leads to dose-related increases of plasma APC and resolution of coagulation imbalances.
Record Date Created: 20030609

17/7/30 (Item 2 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

11917601 99361071 PMID: 10432506
Studies of the relationship between ultrastructural synaptic plasticity and ribosome number in dendritic terminals in the rat neocortex in a cellular conditioning model.
Khludova G G
Department of Higher Nervous Activity, M. V. Lomonosov Moscow State University.
Neuroscience and behavioral physiology (UNITED STATES) Mar-Apr 1999, 29 (2) p175-80, ISSN 0097-0549 Journal Code: 0330471
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The relationship between structural changes in postsynaptic densities of axodendritic synapses and the sizes of postsynaptic ribosomal aggregations were studied. A positive **correlation** was found between the thickness of the postsynaptic density and the number of ribosomes. The role of **dendritic** mRNA and the possible mechanisms supporting rapid local protein synthesis during the modification of postsynaptic components is seen on combined **administration** of two neuromediators into the rat neocortex.
Record Date Created: 19991004
Record Date Completed: 19991004

17/7/31 (Item 3 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09174316 20479264 PMID: 11067334
HCFA's final rule on APCs is out: ED managers can breathe sighs of relief.
ED management - the monthly update on emergency department management (

UNITED STATES) May 2000, 12 (5) p49-56, ISSN 1044-9167
Journal Code: 9425690
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
The final rule on ambulatory payment classifications (**APCs**) for outpatient services from the Health Care Financing **Administration** (HCFA) was published in the April 7, 2000, Federal Register, with a July 1, 2000, implementation date. EDS might receive increased reimbursement for services under **APCs**, in sharp contrast to previous **predictions** of a 15% decrease in reimbursement. Instead of combining CPT and ICD-9-CM coding for clinic and emergency visits **APCs**, HCFA has assigned three **APCs** for the emergency department and a fourth **APC** for critical care. There is no **APC** for a medical screening exam, which could improve reimbursement. There is no separate **APC** for observation services, which means no additional payment will be given. You can continue to use your current charge structure and **correlate** present levels of service with the appropriate CPT visit level. You will have to "unbundle" visit levels to list nursing and physician procedures separately as specific line items.
Record Date Created: 20001018
Record Date Completed: 20001018

17/7/32 (Item 4 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

09165644 20468866 PMID: 11016651
Use of two predictive algorithms of the world wide web for the identification of tumor-reactive T-cell epitopes.
Lu J; Celis E
Department of Immunology and Cancer Center, Mayo Clinic and Mayo Graduate School, Rochester, Minnesota 55905, USA.
Cancer research (UNITED STATES) Sep 15 2000, 60 (18) p5223-7, ISSN 0008-5472 Journal Code: 2984705R
Contract/Grant No.: R01CA80782; CA; NCI
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
Tumor cells can be effectively recognized and eliminated by CTLs. One approach for the development of CTL-based cancer immunotherapy for solid tumors requires the use of the appropriate immunogenic peptide epitopes that are derived from defined tumor-associated antigens. Because CTL peptide epitopes are restricted to specific MHC alleles, to design immune therapies for the general population it is necessary to identify epitopes for the most commonly found human MHC alleles. The identification of such epitopes has been based on MHC-peptide-binding assays that are costly and labor-intensive. We report here the use of two computer-based prediction algorithms, which are readily available in the public domain (Internet), to identify HL4-B7-restricted CTL epitopes for carcinoembryonic antigen (CEA). These algorithms identified three candidate peptides that we studied for their capacity to induce CTL responses in vitro using lymphocytes from HLA-B7+ normal blood donors. The results show that one of these peptides, CEA9(632) (IPQQHTQVL) was efficient in the induction of primary CTL responses when dendritic cells were used as antigen-presenting cells. These CTLs were efficient in killing tumor cells that express HLA-B7 and produce CEA. The identification of this HLA-B7-restricted CTL epitope will be useful for the design of ethnically unbiased, widely applicable immunotherapies for common solid epithelial tumors expressing CEA. Moreover, our strategy of identifying MHC class I-restricted CTL epitopes without the need of peptide/HLA-binding assays provides a convenient and

cost-saving alternative approach to previous methods.
Record Date Created: 20001013
Record Date Completed: 20001013

17/7/33 (Item 5 from file: 155)
DIALOG(R)File 155:MEDLINE(R)

07177830 92040150 PMID: 1682264
Heat-killed Listeria monocytogenes and L. monocytogenes soluble antigen induce clonable CD4+ T lymphocytes with protective and chemotactic activities in vivo.
Brocke S; Hahn H
Institut fur Medizinische Mikrobiologie und Infektionsimmunologie, Freie Universitat Berlin, Germany.
Infection and immunity (UNITED STATES) Dec 1991, 59 (12) p4531-9, ISSN 0019-9567 Journal Code: 0246127
Document type: Journal Article
Languages: ENGLISH
Main Citation Owner: NLM
Record type: Completed
In the present study we attempted to analyze the possibility to induce in mice a T-cell response using killed Listeria monocytogenes in adjuvant. Clearly, nonviable antigen is capable of inducing protective and granuloma-forming T cells in C57BL/6 mice when emulsified in complete Freund's adjuvant. These T cells were cloned in vitro by using antigen and irradiated splenocytes, as **antigen-presenting** cells, and the clones were characterized in vivo. Listeria-specific T-cell clones showed protective and chemotactic activity upon **adoptive** transfer, although some degree of functional heterogeneity among different clones was observed. The heterogeneous in vivo functions could not be **correlated** with the ability of the clones to produce gamma interferon or T-cell growth factor (interleukin-2 and/or interleukin-4). It was demonstrated that an in vivo relevant fraction of listeria-specific T lymphocytes can be induced by nonviable antigen in complete Freund's adjuvant. These results show that the low immunogenicity of heat-killed bacteria is not due to the expression of specific protective T-cell epitopes only by live bacteria.
Record Date Created: 19911224
Record Date Completed: 19911224
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